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*The Nose, Throat and Ear and their Diseases* By 75 American and European Authors. Edited by CHEVALIER JACKSON M. D., Sc. D., LL.D., F. A. C. S., Professor of Bronchoscopy and Esophagoscopy, Temple University and GEORGE MORRISON COATES, M. D., A. B., F. A. C. S., Professor of Otology University of Pennsylvania Graduate School of Medicine. Assisted by CHEVALIER L. JACKSON, A. B., M. D. Clinical Professor of Bronchoscopy and Esophagoscopy, Temple University Octavo of 1177 pages, with 857 illustrations and 27 inserts in colors. Cloth, $13.00 net.

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# CONTRIBUTORS TO THIS NUMBER

CHARLES R. AUSTRIAN M D., Associate Professor of Medicine The Johns Hopkins University; Assistant Visiting Physician The Johns Hopkins Hospital Physician-in-chief Sinai Hospital.

LEWELLYS F BARKER, M D., Professor Emeritus of Medicine Johns Hopkins Medical School; Visiting Physician, Johns Hopkins Hospital

HARVEY G BECK., M D Professor of Clinical Medicine University of Maryland.

E. W BRIDGMAN M D., Associate in Medicine, Johns Hopkins Hospital

THOMAS R. BROWN M D Physician-in-chief of the Gastro-Intestinal Clinic Johns Hopkins Hospital Associate Professor of Medicine, Johns Hopkins University

CHARLES METCALFE BYRNES, M D., Associate in Clinical Neurology Johns Hopkins University; Neurologist, The Church Home and Infirmary; Consulting Neurologist Baltimore Eye Ear and Throat Hospital

NORMAN B COLE, M. D., Assistant Visiting Physician Johns Hopkins Hospital

ERNEST S. CROSS, M D., Baltimore Md

ELMER B FREEMAN, M D., Associate in Clinical Medicine Johns Hopkins University, Assistant Visiting Physician Johns Hopkins Hospital; Physician-in-chief Maryland General Hospital.

JULIUS FRIEDENWALD M D Professor of Gastro-Enterology University of Maryland *Gastro-Enterologist, University of Maryland and Mercy Hospitals.*

T B FUTCHER, M B Associate Professor of Medicine, The Johns Hopkins University Visiting Physician, The Johns Hopkins Hospital Consultant in-chief The Johns Hopkins Medical Dispensary

ERNEST HOWARD GAITHER, M D Associate in Medicine Johns Hopkins Medical School.

GEORGE A. HARROP M D , Associate Professor of Medicine Johns Hopkins University Associate Physician, Johns Hopkins Hospital

LESLIE B HOHMAN M D Associate in Psychiatry Johns Hopkins Medical School Assistant Visiting Psychiatrist, The Johns Hopkins Hospital.

WARFIELD T LONGCOPE, M D., Professor of Medicine Johns Hopkins University; Physician in-chief Johns Hopkins Hospital.

MAURICE C PINCOFFS, M D., Professor of Medicine University of Maryland

C. C SHAW M D Baltimore, Md

THOMAS P SPRUNT M D., Associate in Medicine The Johns Hopkins University Assistant Visiting Physician, The Johns Hopkins Hospital.

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THE MEDICAL CLINICS
OF
NORTH AMERICA

Volume 16 Number 5

CLINIC OF DR LEWELLYS F BARKER

BALTIMORE

## DISCUSSION OF THE NATURE AND RELATIONSHIPS OF MULTIPLE MYELOMA, WITH ILLUSTRATIVE CASE[1]

DURING recent years our knowledge of a group of diseases of the skeletal system that resemble one another in certain particulars has been very carefully studied so that we now have methods of differentiating the different types clinically and can nearly always be sure of a diagnosis *intra vitam*

The patient selected by Professor Pincoffs for the clinic today illustrates very well indeed one of the members of this group I have to thank the clinical clerk, Mr W K. Koenigsburg, for a detailed history of the patient and for reports of the various examinations that have been made

### CASE HISTORY

The patient, George H, a colored man, forty-four years of age, married, was admitted to the University Hospital, Ward D (service of Professor Stein), on November 22, 1932 (eighteen days ago)

Complaints.—Pains in the back, especially on movement, and much gas in the stomach and intestines

Family History.—The patient comes of a long lived family, his father dying at ninety-one, his mother being still alive at eighty He has had four sisters, three of whom are living and

[1] Clinic to Physicians at the University of Maryland Hospital, Thursday December 8 1932

well, one having died of an abdominal tumor He has had five brothers, four are living and well, one brother died of tuberculosis at the age of twenty-one

Past History —Except for measles in childhood, pneumonia at eight, an illness that was probably typhoid at twenty, and two neisserian infections, the patient's past history was uneventful

Present Illness —On April 4, 1931, the patient fell down stairs and hurt his back, after which he had much pain in the back He at first said that he had no pain in the back before wrenching it at the time of the fall, but, later, he told his physician that he had had "colds in his back" four or five months earlier He consulted Dr A A Schaye, of New York, on April 16, 1931, who sent him into the City Hospital in New York City At the end of two weeks in that hospital he felt worse, found that he could not walk or even get out of bed, despite the fact that his back was strapped When Dr Schaye first saw him, he stated that he had had pains in the back for about two months, numbness of the legs for three or four months, and flatulence

While in the City Hospital, Bence-Jones body was found in the urine At the end of three months he could walk again and felt some return of strength, he was discharged on August 27th, after about four and three-quarter months stay in the hospital He was then referred to the Cancer Hospital for *x*-ray examination and there areas were found in the bones that were believed to be due to multiple myeloma He was given *x*-ray treatment to the back three times per week for about five months at the Cancer Clinic Some *x*-ray treatment was applied also over the hips, chest, elbows, and head

The patient says that when the pain in his back is bad he must lie down Sometimes he has pain in his right chest He describes the pain now as a dull, aching, pressure-like feeling

He has also complained much of belching and of "a feeling as though there were bubbles of gas in his back" The presence of the gas, together with any movement, he thinks causes pain

When in the City Hospital he states that there was some weakness of the left leg, but this disappeared later Aside from

some apprehension with regard to his condition, he has manifested no other symptoms He has always been markedly overweight and thinks he has gained more weight recently

Physical Examination.—Marked obesity Lipoma opposite the lateral end of the left clavicle. Mental state clear Slight fever at times but not exceeding 99 5 F One lymph gland palpable in the right axilla, no other lymph gland enlargement Pulse rate 80 No irregularity Blood pressure 136 systolic, 80 diastolic on admission, it has fallen to 100 systolic 60 diastolic since Head negative. No struma Emphysematous type of thorax with hyperresonance and prolonged expiration but no râles Heart and aorta negative Abdominal examination negative except for obesity Deep reflexes of lower extremities somewhat exaggerated No objective disturbances of sensibility No paralyses

Marked kyphosis of lower thoracic spine. Some bowing of the tibia

Laboratory Tests —*Urine*—Specific gravity 1 019 to 1 025, some serum albumin present, and Bence-Jones body present, no sugar, an occasional cast, an occasional white blood corpuscle, no red blood corpuscles, phthalein output, 70 per cent

*Blood*—Red blood cells, 4,080,000, hemoglobin, 85 per cent, white blood cells, 6800 Stained smears studied by Dr J G Huck, showed slight anisocytosis and poikilocytosis Differential count Polymorphonuclear neutrophils, 76 per cent, polymorphonuclear eosinophils, 2 per cent, polymorphonuclear basophils, 0, small mononuclears, 14 per cent, large mononuclears and transitionals, 8 per cent, no myelocytes, myeloblasts, or irritation forms seen, platelets slightly increased, no parasites seen Impression Chronic secondary anemia of hypochromic type (color index 0 7) Wassermann reaction negative.

*Blood Chemistry*—Nonprotein nitrogen, 26 mg per cent, sugar 92 5 mg per cent, chlorides, 270 mg per cent, cholesterol, 208 mg per cent, serum albumin, 4 19 mg per cent, serum globulin, 2 75 mg per cent

Sputum negative Stool negative Basal metabolic rate normal

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Sputum negative Stool negative Basal metabolic rate normal

**x-Ray Examinations** (Dr H J Walton) —*Skull* —A few small, cystlike areas in the flat bones of the skull, sella small and of the closed-in type

*Chest* —Many small, cystlike areas in the ribs, scapulae, and clavicles, areas that are characteristic of myelomata

*Spine* —Destruction of the tenth thoracic vertebral body with marked posterior kyphosis, anterior superior border of the body of $T_{11}$ rests against the center of the lower articular surface of $T_9$, cystlike areas in the bodies of $T_9$ and $T_{11}$ characteristic of myeloma

*Pelvis* —Multiple cystlike areas of myeloma in both ilia

**Diagnosis** —1 Multiple myeloma involving the spine, ribs, skull and pelvic bones, with Bence-Jones body in the urine, and with pain and postural deformities

2 Chronic secondary anemia of hypochromic type

3 Marked obesity

4 Pulmonary emphysema

5 Mild nephropathy with albuminuria and cylindruria and hyperpermeability to phthalein but without increase of blood pressure

## DISCUSSION OF THE CASE

The diagnosis in this patient presents but relatively little difficulty, first, because of the existence of the characteristic syndrome of Kahler's disease (persistent pain, kyphosis, slight fever, Bence-Jones body in the urine, secondary anemia, characteristic a-ray findings in the vertebral bodies, the ribs, the flat bones of the skull, the clavicles, the scapulae, and the pelvic bones)

This typical case will serve as a suitable text for some brief comments upon multiple myeloma, a disease concerning which our knowledge has been vastly increased during the past few years Now that you have seen the patient and heard his history, he may be taken back to the ward, and I shall spend the rest of the hour in a discussion of some of the more interesting features of the disease

**Historical** —H Bence-Jones (1848) described a peculiar protein in the urine of a patient suffering from a skeletal disease

subsequently described by W MacIntyre (1845) as a case of mollities and fragilitas ossium The term "myeloma" was introduced by von Rustitzky (1873), though the Bence Jones protein was not present in the urine in his case A very careful clinical study of the malady was published by Kahler (1889) and, later on, Bozzolo (1898) dubbed it "Kahler's Disease"

Incidence of the Disease in General and Its Occurrence in Baltimore —The disease is far less uncommon than was formerly supposed Reports of cases were slow to appear for many years after the earliest descriptions but as clinicians have grown more familiar with the symptomatology and especially since the application of the x ray to diagnosis in suspect cases ever more cases have been recognized each year In 1928, Geschickter and Copeland made a collective review of some 425 cases and described 13 additional from the Johns Hopkins Hospital, and, in the same year, Drs Perlzweig, Delrue, and Geschickter reported an unusual case of hyperproteinemia associated with multiple myeloma Here, in Baltimore, also Dr Louis P Hamburger had reported 2 cases as early as 1901, Dr W G Macallum had studied the disease histologically, Dr F H. Baetjer had discussed the roentgenological findings and Drs Beck and McCleary (1919) had given an early description of one of the special forms of the disease in which the new growths occur not only in the bones but also in other tissues and a small number of plasma cells appear in the circulating blood

Nature of the Malady —The precise position of the disease in pathologic classification is still in dispute At first believed to be a true tumor, the drift in recent years has been toward the idea of a system disease of the blood making apparatus related to the aleukemias and the leukemias We know now that the myelomata may appear multiply and independent of one another in the bone marrow in different parts of the body, or a myeloma may appear singly and apparently metastasize Moreover, one may meet with diffuse infiltrations of the myelomatous tissue rather than with discrete nodular masses Again, the new tissue may have its origin, apparently, in any one of several immature types of cells in the bone marrow (lymphoblasts,

myeloblasts, plasmocytes, or erythroblasts) Growths (either secondary or primary) may also appear in extra-osseous tissues (lymph glands, spleen, thyroid, liver, suprarenals, ovaries, dura mater, pituitary gland) as well as in the bone marrow In the early stages of the disease, the white corpuscles of the blood may not increase in numbers, though in the terminal stages a large increase in the white count (lymphocytes, plasma cells, or sometimes myelocytes) may be encountered as though the malady were undergoing transition from an aleukemic into a true leukemic state Obviously, until further light is thrown upon the nature of this obscure process, we shall do best to keep our minds open with regard to its classification

**Clinical Findings**—If we exclude certain somewhat similar cases occurring in childhood, the *age incidence* is approximately that of cancer The disease is observed in *both sexes*, but much more often in men than in women The onset is, as a rule, insidious, with *pain* of one sort or another in the foreground The pains may be described as "rheumatic" or "neuralgic", sometimes, they are mild (with vagueness of description as regards distribution), but in other cases they may be agonizing and be definitely referred to some single bone (jaw, orbit, rib, vertebra, etc) In this early stage there is often failure to recognize the nature of the disease, though, later on, *visible or palpable swellings of the bones*, *spontaneous fractures* of ribs, or *postural deformities* (especially of the spine) will excite suspicion and lead to roentgenological studies Often there is slight *fever*, though not always *Anemia* of secondary type develops, the patients lose appetite and grow weak, the *Bence-Jones protein* appears in the urine in over 50 per cent of the cases, but it should not be forgotten that its absence does not rule out the disease In the *later stages*, most deplorable clinical pictures may be seen, in some, paraplegia because of compression of the spinal cord, in others multiple fractures and shocking deformities, in still others, excruciating pains difficult to relieve even with injections of morphine

***x*-Ray Findings**—In the vertebrae and in the flat bones of the head and trunk (tables of the skull, mandible, clavicles,

scapulae, ribs, ilia) one may see spherical areas that look as though bone had been punched out, areas that vary in diameter from a few millimeters to 2 cm or more Usually, there is no evidence of production of new bone The cortex of the bone may be expanded Spontaneous fractures of ribs and collapse of the bodies of single vertebrae are common

Differential Diagnosis —In the early stages, with pain as the predominant symptom, a disease of the bone may not even be thought of The malady has often masqueraded for months as "*rheumatism*" or as "*neuralgia*" before becoming recognized Even when the reference of the pain to a particular bony site has been striking, the symptoms may be wrongly interpreted as an "*abscessed tooth*," a "*supra-orbital neuralgia*," the "girdle pain ' of *tabes dorsalis*, or a beginning *Pott's disease of the spine* may be suspected

If swellings occur on the ribs, if spontaneous fractures occur, or if deformities of the spine develop, there will no longer be delay in making *x* ray studies and the diagnosis will quickly be made *Osteomalacia* and *Paget's disease* will but rarely offer difficulty in differential diagnosis

The greatest difficulty may arise in the differentiation from *osteoclastic metastatic carcinosis of the skeleton* (especially when no primary cancer has been discovered), but the distribution of the lesions in the bones (*x* rays) will usually be decisive, though in some instances, removal of a bit of tissue for histologic diagnosis may be necessary for differentiation

Generalized fibrous osteitis with multiple cyst formation in bones (*osteitis fibrosa generalisata*) is usually easily distinguishable from multiple myeloma by *x* ray studies and by studies of calcium metabolism (hypercalcemia, increase of dialyzable calcium fraction with hypophosphatemia), an important differentiation since some 10 cases of this disease have been reported as cured through removal of parathyroid adenoma That recognition may be difficult has however been shown by Jones (1931) who has found that the same disturbance of calcium metabolism may sometimes be met with in multiple myeloma

Treatment of Multiple Myeloma —Until recently multiple myeloma was regarded as a hopeless malady leading to exitus

in from one to three years, and the only treatment applied was for symptomatic relief (especially of the pain), or for the prevention of spontaneous fractures During the past few years, however, it has been shown that the myeloma tissue is particularly sensitive to deep $x$-rays and perhaps also to bacterial toxins, it has been possible definitely to prolong life by the application of these measures and some are optimistic enough to believe that cure may occasionally be achieved

In applying $x$-ray therapy, each demonstrable bony lesion is exposed, at intervals of three or four weeks, two or three times, to the action of the rays Porchownik makes use of one third skin erythema dose (180 kv , 2 5 ma , focal distance 23 cm , filter 0 5 Cu + Al, Coolidge tube)

Coley (1931) reports the use of his toxins (derived from the streptococcus of erysipelas and the bacillus prodigiosus) and believes that they are an excellent adjuvant to deep $x$-ray therapy in the treatment of multiple myeloma

Certainly, in view of our previous disappointing experiences in the treatment of multiple myeloma, it would seem well worth while to make a thorough trial of deep $x$-ray therapy, either with or without the use of Coley's toxins in addition Unfortunately, the patient you have just seen has already reached such an advanced stage of the disease that improvement from any therapeutic procedure would seem almost too much to hope for

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## CLINIC OF DR WARFIELD T LONGCOPE

JOHNS HOPKINS HOSPITAL

### THE DIFFERENTIATION OF ACUTE RHEUMATIC FEVER FROM BACTERIAL ENDOCARDITIS

WE will discuss today a patient who brings up a very important question for discussion The differentiation of acute rheumatic fever from bacterial endocarditis

STUDENT The patient is a colored man of twenty five who entered the hospital on October 25th, complaining at that time of painful calves, sore joints, and chills

*Family history* has no bearing on his illness

*Past History*—He has never been very robust Ten years ago patient had acute rheumatic fever, with onset of fever, epistaxis, general malaise and painful joints This lasted six months After that he was told that he had a bad heart He says that he has not had St Vitus dance or any other acute illness Occasionally he has had precordial pain and exertional dyspnea His occupations are cooking and boxing He has given frequent exhibition bouts until the last three weeks Married one year Wife living and well No children, no miscarriages

*Present Illness*—Eight months ago he experienced occasional precordial pain This came on with exposure to cold Three weeks ago he was chilled by sleeping in a truck On the way home he felt very chilly and could not get warm in spite of sitting near a hot stove During the period following this chilling he had progressive weakness and anorexia, felt badly and lost appetite Three days before admission he began to cough and expectorate, two days before admission his wrists, his knees, and ankle joints became painful, the calves of his legs became tender, his ankles began to swell and he was brought to the hospital

Temperature on admission 100 F , respirations 22, pulse 72 Blood pressure 115–124/30–40 Sitting propped up in bed There was a moderate amount of pallor, no cyanosis, no petechiae Fingers of both hands show distinct clubbing He did not have any dyspnea The pharynx was reddened, the tonsils somewhat enlarged, but there was no exudate over them Examination of the eyegrounds showed marked pulsation of arteries Skin was very dry Tongue was coated Tonsils were moderately inflamed There was general glandular enlargement, especially of the epitrochlears Pulsation was noticeable in vessels of neck Chest was flat and long There were a few râles at bases of lungs

The heart was enlarged, apical impulse very forceful, prominent in the fifth interspace 8 cm from midline Over the sternum a faint systolic thrill was felt Dulness 10 cm to left in fifth space, $9\frac{1}{2}$ cm in fourth space, $3\frac{1}{2}$ cm to right in fourth space No retromanubrial dulness At the apex very loud booming first sound followed by a rough systolic murmur transmitted to the axilla The second sound was loud but somewhat blurred, and along the left border of the sternum there was a loud diastolic murmur and much accentuated second sound in pulmonic area In the aortic area sounds were not loud, the second was replaced by a diastolic murmur Pulsations in peripheral vessels were everywhere exaggerated There was a collapsing radial pulse and capillary pulse with pistol-shot sound and Durozier murmur over the femoral artery Radial pulse at this time was regular

Abdomen was scaphoid and soft There was no tenderness Liver margin was not palpable Spleen was not palpable

External genitalia normal Rectal examination showed nothing abnormal Neurological examination showed nothing abnormal

*Blood Count*—Red blood cells, 3,810,000, white blood cells, 12,900, hemoglobin, 65 per cent, polymorphonuclear neutrophils, 82 per cent

*Urine*—Specific gravity 1 019, amber, acid There was no sugar Albumin 2+, numerous casts, many leukocytes, moderate numbers of red blood cells Wassermann reaction was negative

Nonprotein nitrogen of the blood, 80 mg per 100 cc

Cultures from throat showed many streptococci of beta hemolytic type, some colonies of Staphylococcus aureus Repeated cultures from the blood stream showed no growth of

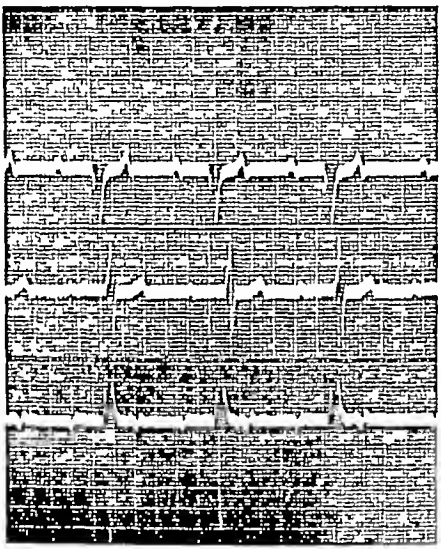

Fig 190—Film No 9995 Date October 26 1932 Rate 54 Rhythm sino-auricular P R interval 0.37 sec. Remarks Normal sinus rhythm Sinus bradycardia. First degree heart block. T III inverted Levogram

bacteria Repeated cultures from urine showed no growth of bacteria

Phthalein excretion, 60 per cent in two hours

On admission it was obvious that the patient suffered from an acute febrile illness, preceded by sore throat and attended by arthritis The physical signs indicated that he had involvement of the mitral and aortic valves with mitral stenosis and insufficiency and aortic insufficiency On admission he was given

aspirin in doses of 3 to 4 Gm a day, and on the day of admission 0 3 Gm powdered digitalis On the 26th he received 0 6 Gm digitalis, on the 27th 0 2 Gm and on the 28th 0 1 Gm digitalis, making in all 1 2 Gm of digitalis in a period of four days In spite of the elevation of temperature on the 25th and 26th to 102 F the pulse rate was slow and varied from 80 to 56 On this account an electrocardiogram was made (Fig 190) which

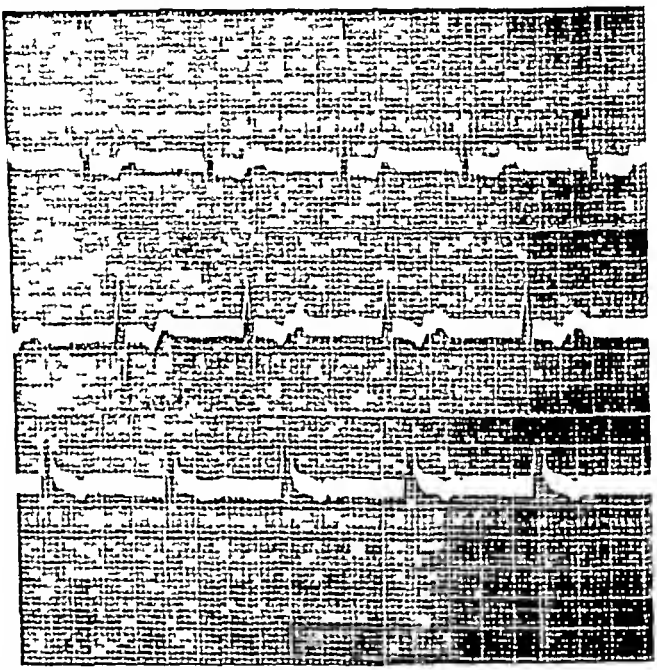

Fig 191 —Film No 9995 Date, October 29, 1932 Rate 71 Rhythm sino auricular P-R interval 0 56 sec Remarks Normal sinus rhythm Sinus arrhythmia First degree heart block. P-R interval is unusually long T waves inverted in all leads

showed a rate of 54, a sino-auricular rhythm, with marked prolongation of P-R interval to 0 37 sec T III was inverted and the electrocardiogram showed the changes indicative of a levogram By this time pain had disappeared from the joints and muscles of legs and the patient felt quite comfortable though the temperature was still elevated The digitalis was, therefore, reduced, as has been indicated, to 0 2 Gm on the 27th and to

0 1 Gm on the 28th On the 28th, pulse rate, in spite of the fact that temperature varied between 101 and 102 F , was recorded as 46 and showed an irregularity suggesting frequent dropped beats Another electrocardiogram was therefore made on October 29th (Fig 191), at which time pulse rate had increased as the temperature rose to 104 F In this electrocardiogram the rate was regular but the delay in conduction time was even

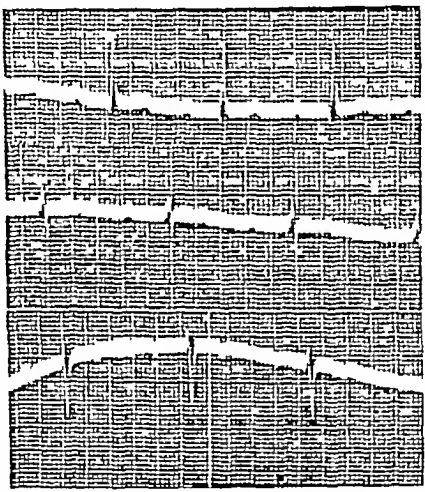

Fig 192 —Film No 9995 Date November 5 1932 Rate 63 Rhythm, sino-auricular P R interval 0.32 sec. Remarks Normal sinus rhythm First degree heart block less marked than on previous record Levogram.

greater than that previously observed, being 0 56 of a second Undoubtedly the irregularity noted at times was due to a second degree heart block Temperature continued between 101 and 104 F until November 11th, when, after daily swings from 103 to 104 to 98 or 96 F , the average temperature fell to 101 to 100 to 98 F At the same time the leukocytes, which had varied between 16,000 and 28,000 gradually fell to from 5000 to 6000,

and marked general improvement occurred During the febrile period repeated blood cultures from both arterial and venous blood and on aerobic and anaerobic media failed to show growth of bacteria On October 31st, beta hemolytic streptococci and Pneumococcus Type IV were recovered in cultures from the sputum There has been a progressive anemia, hemoglobin

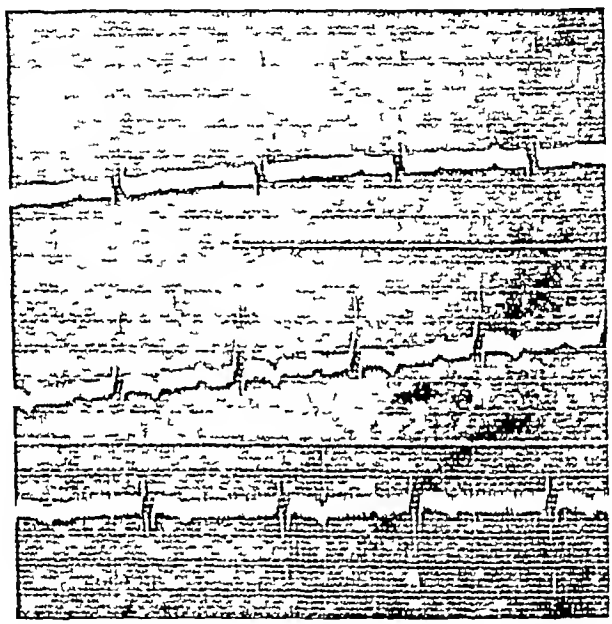

Fig 193—Film No 9995 Date, November 16, 1932 Rate 65 Rhythm, sino auricular P-R interval 0 28 sec Remarks Normal sinus rhythm First degree heart block. T II and III inverted Levogram

reaching 54 per cent and red blood cells 3,000,000 by November 8th

The albuminuria, hematuria, and cylindruria have persisted, though they have diminished with the fall in temperature There has been some variation in the output of phthalein, which on November 12th was 70 per cent On November 7th, the blood nonprotein nitrogen was 33, urea clearance 95 and 130 per cent of normal standard

The first degree heart block, however, has persisted and on November 5th and 16th, eight and nineteen days after the digit-

alis was stopped, the P-R interval was 0 32 second[1] (Figs 192, 193)

The features that are to be particularly remarked upon are the comparatively slow and at times irregular pulse, the almost

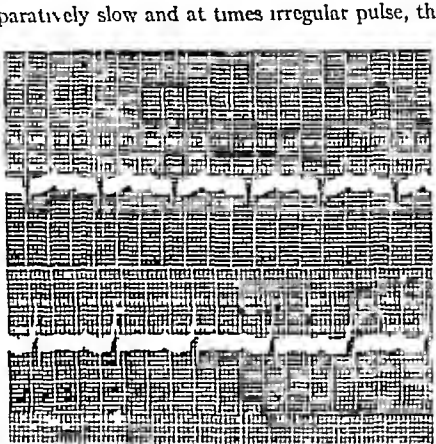

Fig 194—Film No 9995 Date, November 30 1932 Rate 86. Rhythm sino-auricular P R interval 0.27 sec. Remarks Normal sinus rhythm. First degree heart block persists. T III inverted. Levogram

negligible symptoms and signs of cardiac insufficiency, the ab

[1] During the period of patient s illness no tests were made to determine whether the heart block could be affected by atropine. The patient was again seen however by Dr Bedell on November 16th after he had left the hospital and when convalescence was fairly well established At this time, nineteen days after digitalis had been stopped there was still a first degree heart block (Fig 194) with a heart rate of 65 the P R interval was 0 28 sec. After the administration of atropine (Fig 195) rate increased to 111 hut the block persisted P R interval remaining at 0 24 sec.

sence of splenic enlargement, the negative blood cultures, and the symptomatic improvement with fall of temperature and reduction of the leukocyte count

The problem which naturally confronts us is to determine whether this patient is suffering from an exacerbation of rheumatic fever in which the auricular ventricular conduction time is extraordinarily lengthened, either from the effect of the disease

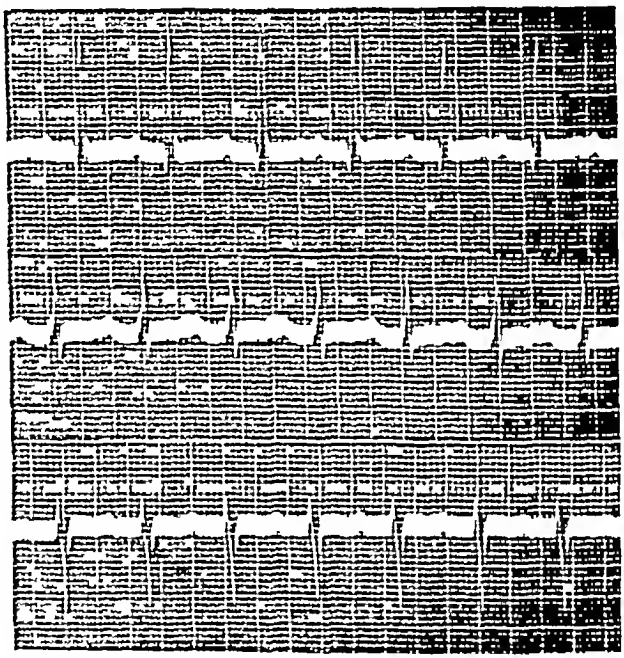

Fig 195—Film No 9995 Date, November 30, 1932 Rate 111 Rhythm, sino auricular P-R interval 0 24 sec Remarks Ten minutes after the administration of 1 mg of atropine subcutaneously, the rate rose to 111 and the P-R interval became somewhat shortened but the first degree heart block was not entirely abolished

process, or from the administration of comparatively small doses of digitalis or possibly from a combination of the two factors, or whether the acute illness is due to bacterial endocarditis, presumably in the bacteria-free stage engrafted upon a chronic rheumatic endocarditis One may cite the following factors which would be unusual in an exacerbation of rheumatic fever First the comparative bradycardia in such a severe

exacerbation, secondly the insignificant evidences of cardiac failure in a patient who shows such pronounced alterations in the mechanism of the heart beat, and thirdly the absence of signs, under these conditions, of involvement of the pericardial surfaces The presence of albumin, casts, red blood cells and leukocytes in the urine is not very uncommon in acute rheumatic fever In most patients these changes are transient, but in rare instances they are indicative of a more or less severe hemorrhagic nephritis, anemia and leukocytosis is common in both conditions Clubbing of the fingers is rarely a sign of acquired heart disease, unless due to bacterial endocarditis

On the other hand, to support the diagnosis of bacterial endocarditis one may call attention to the absence of definite evidence of myocardial failure, the comparative bradycardia, the clubbed fingers, and the changes in the urine, while opposed to this diagnosis is the pronounced symptomatic improvement, the total absence of petechiae in the skin, mucous membranes and retina, the lack of splenic enlargement, the persistent negative blood cultures, and the extraordinarily marked derangement in the mechanism of the heart beat

This peculiar disturbance furnishes us an excellent opportunity to compare with some care the alterations which may take place in the myocardium in rheumatic fever with those that have been observed in the various forms of acute and subacute bacterial endocarditis We may further enquire into the symptoms and signs to which such pathologic changes may give rise

But first it is necessary to determine whether the remarkable prolongation of the auricular ventricular conduction time can be ascribed in this patient to digitalis, to disease of the myocardium, or to a combination of the two A common result of large doses of digitalis is a prolongation of the P R interval in the electrocardiogram, though complete heart block is rare A matter with which you are also familiar, and which we will consider in more detail later, is the frequency of prolongation of the auricular ventricular conduction time in rheumatic fever It is important to remember, however, that the mechanism by which digitalis acts is quite different from that by which rheu

matic fever acts Digitalis produces its effect through the vagus nerves, and the different stages of heart block caused by this drug may be promptly annulled by the administration of atropine Rheumatic fever brings about a prolongation of conduction time probably through the anatomical lesions that it causes in the myocardium, of which these illustrations (lantern slides) furnish good examples This form of heart block is not relieved by atropine

The amount of digitalis which was administered to the patient whom we have seen today was much too small to cause such profound disturbances in the action of the heart of a normal individual, or in one suffering from most forms of heart failure, and the arrhythmia has persisted for a period out of all proportion to the size of the dose, but since atropine has not been given to this patient as yet we are not at liberty to exclude the possible effect of digitalis as contributing to the onset and persistence of the unusual prolongation of the P-R interval It has been recognized, indeed, that patients suffering from rheumatic myocarditis are abnormally susceptible to the effects of digitalis in this respect, and that the exaggeration of a lengthening of the P-R interval may be brought about by comparatively small doses of digitalis in rheumatic patients These effects, however may continue for many days after the patient has ceased to take digitalis Crawford[1] has reported an instance of rheumatic fever which showed an advanced degree of heart block while under treatment with digitalis in usual doses The block increased to periods of complete dissociation for four days after digitalis was stopped, and a severe grade of block continued for fourteen days after the cessation of digitalis The condition was ascribed, in large part, to digitalis, since the block could be broken by atropine, but it is inferred that a rheumatic lesion of the bundle also existed which predisposed to this unusual action of digitalis Unfortunately it was impossible to determine in our patient whether the condition during the acute phase was an-

[1] Crawford, J H Observations on a Case of Heart Block in Acute Rheumatic Fever Under Treatment with Digitalis, Amer Heart Jour, 1927, iii, 196

alogous to that described by Crawford Such a possibility must be seriously considered (Subsequent examination has shown that the heart block was not caused exclusively by digitalis)

We have already seen in lantern slides the lesions in the heart valves the myocardium and the pericardium which are common in rheumatic fever, and we may now turn to a consideration of the myocardial lesions in the various forms of bacterial endocarditis and discuss any possible relationship which these may have, when present, to disturbances in the mechanism of the heart beat In general, lesions in the myocardium are considered to be unusual and of minor importance in bacterial endocarditis Blumer mentions as a special peculiarity of the cardiac lesions in subacute bacterial endocarditis the relatively slight involvement of the myocardium, and it is well known that myocardial failure is not a noticeable feature of this disease, except in its terminal stages In 150 autopsies collected by Blumer,[1] myocardial lesions were described only thirty times, in twelve instances there was fatty degeneration or cloudy swelling, in eight, interstitial myocarditis, in two, acute myocarditis, in three, small abscesses of the heart muscle, in two, focal necroses and in two infarcts

Before we consider this question further, it is well to review the causes of bacterial endocarditis, the forms of endocarditis which they produce and the duration of the disease to which they give rise

The table, which is taken from the recent lectures of Dr Thayer on this subject, furnishes some of this information The more acute forms of the disease are caused especially by the pneumococcus staphylococcus, and gonococcus The lesion in these forms is often ulcerative in nature and when the aortic valves are involved, the ulceration may affect the membranous septum and the adjacent heart muscle As may be seen in the table, myocardial lesions and small abscesses, in particular, are often encountered in the staphylococcus endocarditis Streptococcus viridans, B influenzae and occasionally the gonococcus give rise to the more chronic forms of bacterial endocarditis

[1] Blumer G Subacute Bacterial Endocarditis Medicine 1923 2 105

A vegetative lesion is the rule, but ulcerative lesions may occur It may be seen from the chart that 40 to 50 per cent of the cases collected by Dr Thayer have shown myocardial changes The characteristic one is represented by an area of necrosis surrounded by leukocytes and simulates the Bracht Wachter bodies produced experimentally in the hearts of rabbits by the injection of green streptococci

We may now ask whether these myocardial lesions, described in about half the fatal cases of bacterial endocarditis, may have any influence on the cardiac mechanism In rare instances, such as that referred to by Rothschild, Sachs, and Libman,[1] an ulcerative lesion of the aortic valve may affect the bundle of His and cause heart block

Auricular fibrillation is much less common than in rheumatic fever, but one finds that prolongation of the auricular ventricular conduction time, though more unusual than in rheumatic fever, is nevertheless recorded in a certain proportion of instances As you know, prolongation of the P-R interval has been observed when repeated electrocardiograms are made at frequent intervals (daily or even oftener), in from 50 to 75 per cent of the cases of acute rheumatic fever The incidence which is usually recorded, however, is much less and varies from 25 to 35 per cent It is impossible to know in what proportion of these instances the administration of digitalis may play some part in the delayed conduction The table shows the relative frequency of prolongation of the P-R interval in electrocardiograms from cases of rheumatic fever and from cases of subacute bacterial endocarditis

It may be concluded, therefore, that some form of pathologic lesion may be found in the heart muscle of about one half the cases of bacterial endocarditis that come to autopsy, and that, in a relatively small proportion of instances, alterations in the cardiac mechanism may be detected during life

A degree of heart block such as obtained in this patient must

[1] Rothschild, M A , Sachs, B , and Libman, E The Disturbances of the Cardiac Mechanism in Subacute Bacterial Endocarditis and Rheumatic Fever Amer Heart Jour , 1927, 2, 356

ETIOLOGIC ELEMENT IN 536 CASES INFECTIVE ENDOCARDITIS 306 COLLECTED BY DR THAYER

| | Thayer | Total. | Per cent. | Thayer myocardial lesions. |
|---|---|---|---|---|
| Streptococcus | 191 | 335 | 62 5 | 50% |
| Pneumococcus | 38 | 79 | 14 7 | 45% |
| Staphylococcus aureus | 28 | 60 | 11 2— | 70% |
| Gonococcus | 31 | 37 | 6 9+ | 40% |
| B influenzae (Pfeiffer) | 9 | 14 | 2 6+ | 1 case |
| Staphylococcus albus | 6 | 7 | 1 3+ | 1 case |
| Streptococcus and staphylococcus | | 1 | 0 2— | |
| B pyocyaneus | 1 | 1 | 0 2— | |
| B anthracis | 1 | 1 | 0 2— | |
| B Friedländer | 1 | 1 | 0 2— | |
| | 306 | 536 | 100 0 | |

RELATIVE FREQUENCY OF PROLONGED AURICULAR VENTRICULAR CONDUCTION TIME IN RHEUMATIC FEVER AND BACTERIAL ENDOCARDITIS

| | | Total. | Prolongrd P R interval. | Per cent | |
|---|---|---|---|---|---|
| Levy and Turner (Arch Int Med 1929 43 267) | Rh fever | 403 | 112 | 27 8 | 5 incomplete block |
| | Bact. end | 23 | 3 | 13 0 | |
| Rothschild Sacks and Libman (Amer Heart Jour 1927 2 356) | Rh fever | 65 | 23 | 35 3 | |
| | Bact. end | 61 | 10 | 16 4 | |
| Johns Hopkins Hospital | Bact end. | 21 | 2 | 9 5 | |

be very rare in bacterial endocarditis and it seems probable, in spite of several features in the patient's illness that suggest the presence of bacterial endocarditis in the bacteria-free stage, that we are dealing today with a patient, the subject of long-standing rheumatic endocarditis of the mitral and aortic valves, who is suffering from an exacerbation of rheumatic fever, preceded by an acute pharyngitis and tonsillitis caused by hemolytic streptococci of $\beta$ type The peculiar features of this acute attack are the unusually long conduction time between auricles and ventricles, the comparative bradycardia, the albuminuria, hematuria, and cylindruria together with other changes that often accompany subacute bacterial endocarditis

## CLINIC OF DR JULIUS FRIEDENWALD

FROM THE GASTRO-ENTEROLOGICAL CLINIC OF THE DEPARTMENT OF MEDICINE, UNIVERSITY OF MARYLAND

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# THE FUNCTIONS OF THE STOMACH AS INFLUENCED BY DISEASES OF OTHER ORGANS AND THEIR INTERRELATIONSHIP

THE study of the interrelationship between the stomach and other organs is a matter of considerable interest Not only do affections of the stomach produce symptoms in proximate as well as in distant organs, but the stomach not uncommonly acts as a sensitive gauge often registering even slight disorders due to malfunction of other organs

It is to this interrelationship that I desire especially to direct attention in this clinic

It is easily conceivable why the stomach should he more or less secondarily affected as the result of disease of other organs This may be accounted for by direct contact of a neighboring diseased viscus or may be due to an interference with normal circulatory or nervous mechanisms or be the result of a toxemia

There are but few diseases that are not accompanied to a greater or less degree by gastric manifestations On this account, it is extremely important whenever gastric symptoms arise to institute a complete general investigation of the entire organism in order to discover every possible etiologic factor

The following are among the affections in which gastric symptoms are most commonly prominent

1 Cardiac disease
2 Pulmonary tuberculosis
3 Renal disease.
4 Gallbladder disease.

5 Intestinal disease
6 Endocrine dysfunction
7 Syphilis
8 Diseases of pelvic organs
9 Nervous affections

In this clinic we shall only be able to consider the first two affections

## CARDIAC DISEASE

The close relationship of disturbances of the heart to those of the gastro-intestinal tract has long been recognized It is also well known that certain affections of the heart are accompanied at times with gastro-intestinal symptoms which may become so pronounced that unless an extremely careful examination of the heart be made, an erroneous conclusion may be drawn, the primary condition being entirely overlooked This is especially true in the incipient stages of certain cardiac lesions at a period prior to the stage when the signs of decompensation are revealed On the other hand, it is not uncommon to note, that digestive affections may likewise give rise to various cardiac disturbances such as arrhythmia, tachycardia, or even pseudo-anginal pains

The intimate anatomical relation between the heart and the digestive organs will, to a large degree, easily account for many of these manifestations Due to beginning decompensation of the heart, an early enlargement of the liver is produced as a result of portal stasis, in addition to congestion of the other organs in the abdomen and, in consequence, changes in the gastric secretion and motility occur resulting in the production of dyspeptic symptoms With the gastric distention thus brought about, the diaphragm is encroached upon, being forced upward, which may occasion additional embarrassment to the heart, further interfering with its function As a result, a vicious circle is produced which, to a still greater degree, interferes with the digestive functions An intimate relation between the heart and digestive system is also brought about through the nerve supply Both organs are supplied by the vagus and sympathetic systems and any disturbance of the heart may be reflected through these

paths to the stomach interfering with its motor as well as its secretory functions

Finally, as a result of the fermentation and absorption of abnormal products from the digestive tract, the heart muscle may become weakened and in consequence its normal function disturbed

Three elements, (1) pressure from gas, (2) reflex nervous influences, and (3) the result of absorption of toxic substances from the intestinal tract, may all act singly or together in producing these abnormalities

In the study of the interrelation of digestive disturbances to those of the heart, a subdivision into the three following groups may be made as a matter of convenience

1 Digestive symptoms occurring in heart disease

2 Symptoms occurring in relation to the heart due to digestive disorders

3 Symptoms produced by combined disease of the heart and digestive organs

1 **Digestive Symptoms in Heart Disease**—During the stage of compensation in valvular heart disease the digestive functions ordinarily remain normal When decompensation, however, takes place, symptoms directed to the digestive tract are frequently manifested which become more marked as the cardiac dilatation progresses

The two following cases present the relationship between cardiac disease and disease of the stomach

K. M , male, aged fifty-one years has had an old mitral lesion with cardiac hypertrophy since his twelfth birthday when he had an acute rheumatic infection This has produced but slight disturbance of his health until two years ago when he first noted shortness of breath upon exertion and especially in ascending stairs This symptom has gradually become more pronounced and has recently been observed when reclining in bed on retiring at night necessitating the use of three pillows, a procedure heretofore unnecessary In addition there has been palpitation together with an absolute lack of appetite eructations, pressure and fulness following meals and occasional vomiting The pa-

tient also complains of abdominal distention and of occasional abdominal pain The digestive symptoms have been so intense recently that he consulted a gastro-enterologist believing his condition to be due entirely to some digestive affection

On examination evidence of cardiac dilatation and decompensation is noted The heart is found to be markedly enlarged and rapid (rate 110 per minute) and a loud rough systolic murmur is heard at the apex Blood pressure 185/90 A few moist râles are heard at the bases of both lungs The liver is somewhat enlarged and tender on pressure and a slight amount of fluid can be detected in the abdomen There is also a moderate edema of the extremities The blood chemistry and urine examinations are reported to be normal

The diagnosis of cardiac decompensation is evident Treatment consisted of rest in bed, the usual medical measures directed to the cardiac affection including at first a Karell diet together with digitalization Under this therapy the gastric symptoms rapidly disappeared and cardiac compensation followed In about six weeks, on a carefully restricted regimen he will probably again be able to pursue his professional activities as an attorney-at-law

The following case presents the very reverse condition

A K , female, aged forty-six years, has been affected with nervous indigestion in the form of fulness and pressure in the stomach and loud noisy eructations, together with irritability, headaches, and insomnia as the result of a nervous strain due to a prolonged and fatal illness of her husband Recently she has become greatly alarmed by the palpitation and irregularity of her heart following meals in addition to acute pains over the precordium She has lost 15 pounds in weight, is unable to take a sufficient amount of food, is extremely weak and is definitely convinced that she has developed a serious heart lesion

On examination no evidence whatever of a cardiac affection is noted The heart is normal in size and no murmurs can be detected, pulse 96 She is of the visceroptotic type The stomach is rather distended and low in position and a splashing sound can easily be elicited in the gastric area The gastric secretion

shows a rather low acidity, total acidity 30, free hydrochloric acid 16 following an Ewald test meal An *x* ray examination showed the heart normal in size and other than a maximum enteroptosis no abnormality could be detected in the abdomen The basal metabolic rate is normal The blood chemistry is likewise normal and the blood picture reveals a mild secondary anemia

The diagnosis is gastric neurosis with secondary cardiac symptoms Under rest treatment of about six weeks' duration in the hospital, these patients almost invariably gain weight and are entirely relieved of all symptoms gastric as well as cardiac

*Discussion*—*Symptoms*—In cardiac disease in which compensation has been fully established, gastric disturbances are rather rare, though even in these cases we, at times, observe an accumulation of gas in the stomach producing pressure and fulness in the epigastrium, especially following meals in addition to anorexia and eructations Sudden and excessive distention of the stomach and intestine occasionally occurs, which by pressure upward on the heart adds an additional burden to this organ leading to aggravated forms of dyspnea, vertigo and syncope In some instances, extreme palpitation occurs following meals, followed by vertigo and arrhythmia

As the stage of decompensation progresses severe anorexia may develop and, in consequence, the heart is further weakened Not infrequently nausea and vomiting occur providing further difficulties in nourishing the patient, as well as in the administration of the necessary medication The vomitus consists of bile stained mucus often containing traces of blood Rarely hematemesis may occur If vomiting becomes persistent, acidosis is apt to occur with the odor of acetone to the breath The abdomen becomes distended and tender on pressure, the liver enlarges and the skin and conjunctivae are jaundiced In certain instances of cardiac disease associated with general arteriosclerosis, abdominal pain develops as a prominent feature. It is usually of a paroxysmal type, and may extend over a shorter or longer period of time This is frequently associated with abdominal tenderness and pulsation both of which are usually

increased on exertion There is also often present abdominal distention, eructations, pressure and fulness following meals Similar findings are also frequently observed in cases of myocardial disease The same symptoms have also been observed in athletes and in robust individuals past middle life, who have undergone unusual physical exertion, in whom distress in the region of the stomach dizziness and anorexia occur These symptoms are often markedly increased on exertion In cardiovascular disease, attacks of acute cardiospasm are noted frequently associated with intense pain in deglutition and with dysphagia In angina pectoris gastric upsets are not infrequent As a matter of fact, the pain of this disease following upon meals at times associated with distention and eructations may render the diagnosis difficult, and in some instances it may be impossible, unless the patient be held under close and prolonged observation, to determine whether we are actually dealing with a definite anginal affection or a so-called "pseudo-angina pectoris" In considering angina pectoris, attention must also be directed to those cases in which attacks of such severity occur, as to cause death due to injudicious eating

Attention must also be directed to a group of cases of coronary thrombosis in which there is, at times, a close resemblance of the cardiac disturbance to some serious abdominal surgical emergency In some instances, the condition closely simulates cholelithiasis, at times, the pain of coronary occlusion may be confined to the abdomen although in most instances it is noted in the chest The pain, however, is usually more constant and does not occur in attacks Enlargement of the liver and jaundice may occur in both affections and render additional difficulty in diagnosis Occasionally, the electrocardiogram may assist in the differentiation

There is a condition termed "splanchnic dyspepsia" which is characterized by a low blood pressure, large mobile pupils, variability in the pulse rate, vasomotor skin disturbances, and sinus arrhythmia, indicating a disturbance of the circulatory system There are frequently, in addition, other symptoms such as faintness, dizziness, sighing respirations, constipation, gaseous

distention and signs of biliousness and auto-intoxication These symptoms are markedly relieved by rest but are increased on exercise They are also temporarily relieved by laxatives or enemata, as if the condition were due to an intestinal stasis This explanation is, however incorrect inasmuch as relief occurs before evacuation of the bowels has taken place and the symptoms recur within a few hours before stasis could recur

Heart affections, as well as blood vessel changes, play a definite rôle in the formation and development of peptic ulcer In many of these cases occurring in individuals past the sixtieth year of life, serious gastric hemorrhages frequently occur Gastric hemorrhages may also occur in heart affections in which decompensation has taken place, as well as following severe arterio sclerotic changes in the abdominal blood vessels

Liver involvement as the result of chronic heart disease is revealed by an enlargement of the liver with or without jaundice The damming back of the blood necessarily embarrasses liver function, damaging liver cells by compression In consequence of these changes, biliary secretion and excretion is impeded from pressure on the ducts and many microscopical and gross changes are noted in the liver The symptoms observed are dull pain in the liver region with a sense of weight and pressure, together with indigestion, often increased by fats and sweets, loss of appetite, nausea, vomiting, headaches, jaundice, abdominal distention, dyspnea, and edema A casual examination of the heart may reveal but little or very much Usually there is a diminished heart rate at first, though finally it becomes rapid The heart sounds are usually distant and feeble and arrhythmia is usually present

As the result of functional affections of the heart, gastric disturbances are not uncommon as, for example, those noted in instances of tachycardia and in the arrhythmias The stomach manifestations are those of gaseous distention which may become marked together with violent eructations In these cases the relief of the cardiac affection is aided by treatment of the stomach, and the cure is brought about by a careful supervision over the nervous system

In cardiac disease, the degree of gastric acidity depends largely upon the stage of cardiac failure In the early stages of decompensation free hydrochloric acid can ordinarily be observed in the gastric contents, but this gradually diminishes as the condition advances As the acid vanishes, the ferments also begin to disappear, but both may return when compensation has again been established, provided the condition has not been sufficiently prolonged to produce marked anatomical changes in the gastric mucosa In those instances, however, in which it has been prolonged and, especially when it is accompanied by evidences of edema the gastric acidity continues to remain absent

2 Symptoms Occurring in the Heart Due to Digestive Disorders —It is well known, that even in health the ingestion of abnormally large meals or indiscretions in diet may increase the rapidity of the heart beat, and that certain digestive disturbances frequently induce pain around the heart simulating cardiac lesions On this account, if no definite cause for a disturbance of the heart is noted in the heart itself, one's attention should at once be directed to the digestive tract, disturbances of which not uncommonly produce cardiac symptoms These appear in the form of tachycardia, arrhythmia, bradycardia, and even pseudo-anginal pains

Occasionally bradycardia or arrhythmia are observed as a result of gastric disorders and may be greatly intensified by an increase in the digestive symptoms, disappearing with improvement of the condition Increased gas formation with inability to expel it will frequently account for these symptoms

At times angina-like paroxysms may be observed in susceptible individuals due to overeating These are not uncommonly of the pseudo-anginal type and may be entirely corrected by the regulation of the diet They usually occur after a full meal, and are associated with flatulency True angina pectoris at times cannot be entirely excluded until the angina-like symptoms have completely disappeared following treatment of the dyspepsia

Palpitation may be directly occasioned by disease of the stomach and bears a close relation to the gastric digestion, being relieved by correction of the digestive disorder In many in-

stances the expulsion of gas brings about immediate relief In this condition the stomach is often distended and becomes tympanitic This undue stretching, inhibiting the action of the vagus, is thus a potent cause of cardiac disturbance

In other instances the palpitation appears in the early morning arousing the patient from sleep, the stomach is markedly distended by gas and relief is afforded by eructations as well as by direct treatment to the digestive disorder In others, tachycardia occurs during the night, preventing sleep and is not uncommonly associated with dyspnea It occasions great alarm to the patient and disappears not infrequently spontaneously, or following the administration of nerve sedatives In this connection attention must be directed to the condition known as acute pneumatosis which is frequently produced by a simultaneous cardio- and pylorospasm, and which is marked by an extreme distention of the stomach. In this affection, which at times assumes a picture of an alarming nature, dyspnea, precordial discomfort and pain, together with a weak, rapid and irregular pulse and cyanosis are frequently noted Immediate relief is afforded by the expulsion of gas following the introduction of the stomach tube.

It is well known that in certain liver affections, especially those accompanied by jaundice, particularly in the early stages, the heart action fails with the production of a lowered pulse rate In cholelithiasis the acute gallbladder colic may manifest itself at times as pain in the cardiac region occasionally producing symptoms not unlike those observed in angina pectoris In some of these instances prolonged observation may become necessary in order to clear up the diagnosis.

The influence of digestive disturbances upon the heart should be, therefore, constantly borne in mind, inasmuch as the symptoms produced associated with the heart can only be overcome by proper treatment to the gastro-intestinal tract.

3 Symptoms Produced by Combined Disease of the Heart and Digestive Organs —In the study of combined disease of both the heart and the digestive organs, it is important to differentiate between those conditions in which the functions of either

one are disturbed due to the other and those in which both are affected simultaneously independently of each other It not uncommonly happens following prolonged disease of the heart or of the digestive organs, that organic changes in both may become so pronounced as to render it difficult at times to determine the seat of the primary affection

In many of these instances not only does the liver present chronic changes, but permanent gastro-intestinal damage of a rather severe type is produced in the form of catarrh Notwithstanding at least a partial restoration of compensation, the gastro-intestinal tract remains permanently disabled and symptoms such as lack of appetite, abdominal discomfort, nausea and vomiting, alternating constipation and diarrhea, persist An examination of the gastric contents at this stage will reveal an achylia with considerable mucus and much mucus will also be observed in the stools

An acute disease of the stomach or a chronic affection may cause decompensation in a heart in which mild muscular disturbance exists, producing serious manifestation of heart failure, or may even cause attacks of angina pectoris in individuals predisposed to this affection

In nervous individuals gastrocardiovascular symptoms are not uncommon In a certain group of these cases often associated with aerophagia, the condition is paroxysmal The attacks begin and end suddenly, lasting a few hours to two or three days They are mainly observed in the early morning before the patient arises, or they occur during the night and are associated with palpitation, oppression around the heart, fulness, and distention in the epigastrium The patient becomes weak and depressed and dyspnea is marked The attacks recur at intervals, or the affection may become continuous and chronic The condition is commonly observed in neurasthenic individuals, the attacks often recurring following the ingestion of indigestible food During the intervals between the attacks the circulation and heart are normal The cardiovascular paroxysms may be controlled by proper treatment directed to the nervous and the digestive systems

In a further group, also occurring in neurasthenic patients especially in chlorotic females, the symptoms are produced by the ingestion of indigestible food and begin with attacks of slight dyspnea and substernal oppression A gallop rhythm may de velop and the attack is frequently accompanied with pain extend ing into the thorax and the abdomen It may be of varying degree of severity and frequently ends abruptly The heart at no time presents evidence of organic disease

Attention must be directed to the visceral arteriosclerosis occurring during middle life and old age associated with the digestive tract and heart which has, in our experience not been accorded sufficient importance This condition occurs much more frequently than is usually acknowledged

Arteriosclerosis leading to gastric disturbances associated with cardiac disease may be observed in one of two distinct types

1 Those instances in which the arteriosclerotic changes are most marked in the stomach and heart

2 Those in which the manifestations are secondary to a general arteriosclerosis The main clinical gastric manifesta tions, recognized in middle life and old age as the result of car diosclerosis and of arteriosclerosis of the abdominal arteries may be divided into three groups

(*a*) The dyspeptic and cardiac symptoms due to general arteriosclerosis

(*b*) Abdominal angina

(*c*) Gastric ulcer with or without hemorrhage

(*a*) **Dyspeptic and Cardiac Symptoms Due to General Arteriosclerosis**—These symptoms usually begin insidiously and are principally manifested in the form of flatulency, fulness, distention, nausea, eructations, dizziness, palpitation, and short ness of breath At first but a few of these symptoms are noted, and then only on awakening in the morning and they are often relieved by eructations of gas The appetite for breakfast gradually diminishes and the patient finally is unable to eat until the noon meal While the noon meal may be taken with relish the symptoms above mentioned are apt to return in the

afternoon and epigastric distress is not uncommon As time goes on, the general abdominal distention, distress, and eructations are constantly at hand Nausea and retching after meals are not infrequent, but vomiting is rarely noted Tachycardia, dyspnea, and tightness of the chest are not uncommon, adding further to the distress of the patient The flatulency, at times, increases in severity, especially at night and the patient is forced to sit up in bed in great discomfort making efforts to eructate and often suffering with marked dyspnea The night attacks are frequently increased by the evening meal, and on this account, the patient frequently places himself upon a liquid or semisolid diet The symptoms just noted may exist with varying degrees of intensity for years and may even disappear for a short period of time to return often with great severity At this period, however, the dyspnea, flatulency and epigastric distress appear on slight exertion, even without relation to food Intestinal flatulency and distress now manifest themselves and the patient loses weight and strength, the symptoms progress and the patient may die either from an intercurrent cerebral, cardiac or renal complication or from exhaustion

(*b*) **Abdominal Angina**—Abdominal angina occurs frequently as the result of an abdominal endarteritis These changes of an inflammatory or degenerative character take their onset slowly in the abdominal aorta and its branches, are progressive, and are the cause of ill-defined, though often severe abdominal pain This pain is usually paroxysmal in character, is often increased on exercise, is relieved by rest, and is associated with tenderness on pressure along the aortic plexus and with lancinating pains extending along the course of the iliac and femoral vessels

The pain caused by arteriosclerotic changes in the abdominal aorta may be observed in the epigastrium, thorax, or lower abdomen Like angina pectoris, it is ordinarily increased on exertion or excitement, and is accompanied with tachycardia and hypertension The pain is often transmitted into the dorsal and lumbar regions of the spine and disappears under the influence of rest and the administration of the nitrites

(*c*) Gastric Ulcer, With or Without Hemorrhage.—The character of the formation of these ulcerations is of importance. They are definitely due to degenerative changes as a result of marked ischemia of certain parts of the gastric wall caused by an arteriosclerosis (often a thrombo-angiitis of a branch of the gastric artery). A frequent cause of the hemorrhages is found in the rupture of the miliary aneurysms in the small gastric arterioles.

When, in individuals in advanced years with evident manifestations of cardiosclerosis, the usual signs of ulceration occur, one should always suspect the presence of the former affection. On the other hand, inasmuch as carcinoma may have its onset in a similar manner, the diagnosis may become more complicated.

When hemorrhage occurs with ulcer the diagnosis is relatively simple, though as has already been noted, hemorrhages of a massive degree may occur as a result of the rupture of the arteriosclerotic vessels in the stomach.

In order to arrive at a correct diagnosis of this affection, a thorough physical examination of the patient should be made and not too much reliance should be placed upon the mere symptoms of indigestion.

In a patient of middle age or advanced years complaining of flatulency, distention, and with epigastric pains and dyspnea which are relieved by eructations, especially when these symptoms are aggravated at night, a careful examination into the cardiovascular system should be made. Not infrequently one will find marked hypertension with an enlarged heart, with an accentuated second aortic sound or a murmur over the aorta, pulsation in the episternal notch, discomfort on pressure along the abdominal aorta, together with an increase in the urine which is of low specific gravity and contains albumin and casts. These findings point directly to the arteriosclerotic changes as causative factors in the production of the gastric affection.

Finally, attention must be directed to the group of cases in which two entirely distinct affections, one associated with the heart and the other with the digestive tract, may occur independently of each other. Thus a cardiac lesion may have ex

isted for a long period of time and decompensation finally occurs In some of these instances the sudden development of a lesion in the digestive tract such as, for example, carcinoma may render the diagnosis extremely difficult It may be quite impossible, at first, to determine whether we are dealing with a secondary digestive disturbance brought about by a failing heart, or whether the symptoms point rather to a beginning carcinoma of the digestive tract

A similar problem presents itself in patients with digestive symptoms such as are observed in gallstone colic in which anginal attacks likewise occur In both of these groups great difficulty in diagnosis is presented and, at times, the more serious affection may be entirely overlooked In the study of cardiac and digestive affections, it is, therefore, of importance to bear in mind the reciprocal relation of these organs to one another in order to prevent serious errors in diagnosis

*Treatment* —The treatment should be directed to the cardiac lesion when this is the primary disturbance This consists of rest in bed, avoidance of overexertion and the use of medicinal cardiac measures The gastric symptoms are best influenced by diet which should be restricted Proteins should be prescribed in moderate amounts and starches should be allowed in limited quantities The meal should be small in quantity and intermediate feedings should be prescribed Ordinarily, liquids should be reduced Enemata are useful in relieving abdominal distention Soda or magnesia or an alkaline laxative in the morning give relief The spirits of chloroform mixture with or without soda when taken in hot water is often helpful in overcoming gas pressure at least temporarily When the cardiac symptoms are secondary to the digestive disturbance, treatment directed to the latter condition will, in all likelihood, bring about relief

## PULMONARY TUBERCULOSIS

Two cases are here presented which, though affected with the identical disease, differ markedly in their symptomatology

L S , male, aged twenty-two years, in previous splendid health, though with a family history of tuberculosis, returned

home after a year's hard work at college for his summer's vacation He had lost his appetite during his last two weeks at college and was occasionally nauseated but attributed these symptoms to the nervous strain of his examinations For the following four weeks the same manifestations continued and a loss of 7 pounds was noted He now began to suffer pain and discomfort in his stomach became constipated had severe nausea and occasionally vomited after forced feeding The pain often appeared several hours following meals A slight hacking morning cough which the patient had not noted was observed occasionally by his brother

On examination the patient presents the appearance of having lost flesh There is some impairment of the percussion note at the apex of the left lung where now and then a few râles can be heard after deep inspiration The lungs are otherwise normal The abdomen presents no abnormalities except the presence of a slight tender epigastric area On *x* ray examination a small lesion is reported in the left apex but the lungs are otherwise clear A gastro-intestinal *x* ray series was reported to be negative The urine is normal, the blood picture shows a slight secondary anemia The sputum contains numerous tubercle bacilli

This case illustrates how easily the initial stage of pulmonary tuberculosis can masquerade under the signs of a gastric disturbance This patient will be sent to the mountains for three months and I predict that he will gain weight and recover

Quite in contrast to this case is the following one

T L, female, aged thirty three years who likewise gives a tuberculous family history In brief, she has presented marked evidences of pulmonary tuberculosis for the past four years There is present a severe cough, a temperature of 101 to 102 F at night, night sweats, and great emaciation The diagnosis has been confirmed by physical, roentgen ray and sputum examinations In addition, however, the symptomatology like wise involves the digestive tract and the patient presents definite signs of a terminal dyspepsia There is present a complete anorexia associated with nausea and occasional vomiting The

vomiting not only occurs following ingestion of food but likewise in the morning being then induced by cough The vomitus contains large amounts of mucus There is present a constant discomfort in the gastric region and fulness, distention, and flatulency are persistent The bowels are either constipated or diarrheic and the diarrhea has led to extreme exhaustion

The emaciation as you see is now extreme and an examination of the abdomen reveals evidence of a marked enteroptosis with relaxation and tenderness in the epigastrium and along the course of the colon An examination of the gastric contents reveals an achlorhydria, total acidity 24, free hydrochloric acid 0, following an Ewald test meal

An x-ray examination of the digestive tract gives no evidence of any defect in the stomach or duodenum However, the spastic irritability with the defect in the proximal colon indicates the presence of a tuberculous lesion in this area

Discussion —The contrast between these 2 cases is marked In both, dyspeptic symptoms are prominent In the first—initial dyspepsia—they occur early and often overshadow the primary lesion, in the second—terminal dyspepsia—they are so intense as to seriously complicate the primary disease When the dyspeptic symptoms are firmly established in the latter condition they usually progress and may in themselves account for a rapid termination

The treatment of this type of case will be given later

The secondary gastric disturbances due to pulmonary tuberculosis are of unusual interest This is due largely to the fact that in this disease, especially in its incipiency, the primary symptoms are frequently entirely gastric in character and consequently often overshadow the pulmonary signs Although the stomach is ordinarily exempt from the lesions of tuberculosis, yet dyspeptic symptoms are frequent in this disease These manifestations may be of two distinct types the initial and the terminal dyspepsias While many causes have been named there can be little doubt that in the initial stages even when a rise in temperature is entirely absent, toxemia may play an important rôle in the production of dyspeptic symptoms

1 Initial Dyspepsia —Dyspeptic symptoms are observed in about 70 per cent of cases of early tuberculosis, but the development of these manifestations is dependent largely upon the sex of the patient, type of pulmonary involvement and the previous state of the digestive tract A majority of patients having pulmonary tuberculosis are affected with indigestion Alcoholics and those individuals who have previously consumed food inordinately are apt to suffer most difficulty in this respect

The digestive symptoms become more marked in those instances in which the pulmonary tuberculosis originates insidiously and progresses gradually In the very acute forms, as in miliary tuberculosis, while gastric symptoms are always present, appearing early and prominently, yet as the pulmonary manifestations become intensified these symptoms are overshadowed to such a degree that they assume but a minor rôle In the more chronic variety, however, inasmuch as the pulmonary symptoms are not as yet pronounced at this stage, the patient's attention is centered more fully upon his digestion and he is on this account more likely to attribute such conditions as loss of flesh and weakness to the gastric disturbance

Females are more susceptible to indigestion than males The symptoms usually manifested during the stage of the initial dyspepsia are loss of appetite, nausea, vomiting, pain and discomfort in the abdomen and constipation

*Loss of Appetite* —Loss of appetite is extremely common and not infrequently marked anorexia occurs This is especially noted when severe constitutional symptoms develop Many patients have a lack of appetite, but notwithstanding this succeed in forcing food Others frequently continue to retain a normal desire until food is served, when this quickly disappears Desire for food is frequently influenced by fever and is often especially lacking in the evening, when the temperature is at its height There is an especial repugnance for fatty foods in this condition

After the dyspepsia has become more chronic, the appetite may become capricious, the same foods being relished at one time and not at another, or the appetite may be normal at one

meal and not at another or on one day and not on another The taste may be altered in other instances and there may be a desire for foods which were previously distasteful, a craving being often developed for acids, such as acid fruits, pickles, and vinegar

*Nausea* —Nausea is not infrequent and may be present as a premonitory symptom before the signs in the chest are sufficiently developed for diagnosis It may persist off and on during the entire course of the disease and resist all means of treatment This symptom may occur early in the morning and may finally result in vomiting, though this does not always follow, or it may appear at any time of the day It is increased when the patient is subjected to forced feeding and is at times induced by coughing and during the periods of increased temperature

*Vomiting* —Vomiting may appear without nausea and is most frequent on arising in the morning due to an irritation in the throat or to paroxysmal cough induced in an effort to expel mucus Under these conditions it in no way interferes with the digestion of food following its subsidence However, in the more chronic types it may follow nausea appearing after meals, but it may even then be associated with cough, which may add materially to the difficulty in feeding the patient On the other hand, vomiting may occasionally precede all other symptoms Forced feeding often induces emesis which likewise occurs at times when the temperature rises in the evening The vomitus consists mainly of undigested food and ordinarily contains a considerable admixture of mucus When the vomiting becomes excessive it may also contain bile Nausea and vomiting may persist even though the disease becomes arrested Ordinarily, however, these symptoms disappear when this takes place

*Pain and Discomfort* —Pain is a rather frequent symptom at this stage, It is not uncommonly associated with discomfort and fulness and distention appearing after meals, though occasionally it occurs independently of food intake It may appear several hours after meals and when associated with symptoms of hyperacidity may lead to an erroneous diagnosis of duodenal ulcer In the very early stages of this affection, the pain may

only be associated with a single meal but as the disease progresses it becomes rather constant The pain may be referred to the epigastrium though it frequently radiates into the chest in the region of the heart and under the lower sternum It may be intimately associated with the change in gastric acidity When the acidity is high it is commonly accompanied with heart burn and acid eructations, and when low it occurs immediately following meals and is often relieved by the use of adequate doses of muriatic acid

*Constipation* —This is a very frequent symptom in the initial dyspepsia of pulmonary tuberculosis It is at times extremely persistent and difficult to overcome The stools are usually light in color, covered with much mucus and contain considerable undigested food remains Intercurrent attacks of diarrhea may occur which become more frequent as the disease progresses

*Physical Examination of the Abdomen* —The physical examination of the abdomen at this stage does not as a rule reveal any abnormalities At times evidences of an enteroptosis are noted, at others, tender areas are detected in the epigastrium or in other portions of the abdomen Atony of the stomach is not an unusual finding

*Examination of the Gastric Contents* —Numerous observations have been reported on the changes in the gastric secretion in this affection Normal gastric contents is usually noted in the incipient cases, while in the slightly more chronic types normal acidity occurs in about 44 per cent of the instances, hyperacidity in about 42 per cent, and reduced acidity in about 14 per cent The motor function of the stomach is usually normal in the early stages, but is reduced with the progress of the disease

It is an interesting fact that tubercle bacilli can commonly be obtained from the fasting stomach in individuals affected with incipient pulmonary tuberculosis, often before the definite physical signs of the disease are revealed Roentgen ray studies in the cases of initial dyspepsia rarely reveal lesions in the stomach or duodenum There is no evidence of the hyperperistalsis

and hypertonicity of the colon which is commonly observed in the advanced cases

*Course and Prognosis*—The prognosis of the initial dyspepsia is largely dependent upon the progress of the pulmonary lesion If the disease is arrested, the dyspepsia will ordinarily disappear, if it advances, however, the gastric disturbance will also become more aggravated, though its character may become altered under these conditions

2 **Terminal Dyspepsia**—As the tuberculous disease of the lung progresses and the final stage appears with great destruction of the lung tissue, the digestion also becomes more involved and the symptoms of indigestion more pronounced The dyspepsia which was present in the incipient stage may alter its character so that, for example, such symptoms as nausea and vomiting may disappear and be replaced by pain, or the same symptoms occurring in the initial dyspepsia may become intensified or finally the dyspepsia may be entirely overshadowed by the pulmonary symptoms In rare instances, the pulmonary symptoms may remain latent even in this stage and the digestive disturbance may be the entire cause of the patient's complaint

Females are more susceptible to the terminal dyspepsia than males The symptoms manifested during this stage are loss of appetite, nausea, vomiting, pain, and discomfort in the abdomen and disturbance of the bowels

*Loss of Appetite*—The appetite usually decreases progressively until complete anorexia occurs, though occasionally there may be periods when it returns to normal, or is even increased Here, too, as has been observed in regard to the initial dyspeptic type, in some instances, the appetite may even become capricious, the same food being relished on one occasion and not at another The taste may be altered, too, at times and there may be a desire for food previously distasteful, a taste developing especially for acid food There is often a lack of desire for fatty foods and sweets and even when consumed in moderate amounts these will frequently produce indigestion While the loss of appetite may be continuous and extreme, it may occasionally be retained even to the last or be increased A marked increase in temperature

is ordinarily associated with extreme anorexia Increased thirst is usual at this stage and is most frequent between meals It is often associated with a rise in temperature

*Nausea* —Nausea is frequent at this stage and is often associated with lack of appetite and vomiting It may persist during the entire stage and resist all efforts for relief Even following vomiting it may continue It not uncommonly occurs early in the morning and is then induced by cough, though it may appear at any time of the day High temperature and forced feeding usually increase this symptom

*Vomiting* —This symptom may appear without nausea and is then most frequent in the morning, due to attacks of coughing It usually follows nausea, hut may even under such conditions be associated with cough When it occurs following a meal, the food is rejected in an undigested state The vomitus is usually acid and contains large amounts of mucus

*Pain and Discomfort* —While pain in the region of the stomach is not so frequent during the terminal stage as in the initial discomfort is more common and most patients exhibit more or less distress in the form of fulness, distention, or flatulency These symptoms may occur following or be independent of food The pain may be of a burning character in the epigastrium and extend to the chest and is ordinarily increased by pressure in this region.

*Disturbance of the Bowels* —While constipation is most common at first occasional attacks of diarrhea occur, which increase in frequency and become persistent, causing intense weakness and exhaustion They are often intractable and resist all means of treatment and in themselves may be responsible for bringing about an earlier termination of the disease The stools are usually light in color and even when solid contain mucus and undigested food particles, even before the stage of tuberculous ulceration of the bowel occurs

*Physical Examination of the Abdomen* —As the disease progresses and emaciation becomes more and more pronounced, evidence of enteroptosis with atony of the stomach becomes pronounced. The examination of the abdomen will disclose

varying conditions according to the extent of the secondary involvement of the intestine as well as of other organs with the tuberculous disease In cases of moderate severity in which there has been as yet but a slight or no secondary invasion of these organs, the abdomen is usually soft, relaxed, and extreme tenderness will be manifested in the epigastrium, and at times along the course of the entire or portions of the colon Even at this period a slight enlargement of the liver with tenderness in this area may be noted A gastric catarrh is by this time almost invariably present As the disease advances, however, the ravages of the secondary involvement become evident, depending largely upon the degree of invasion The abdomen becomes rigid, distended, and evidences of free fluid in the abdominal cavity are manifested and extreme tenderness and pain are observed on palpation

*Examination of the Gastric Contents*—The stomach in the stage of terminal dyspepsia ordinarily presents a high grade of motor and secretory insufficiency These changes may occur due to the production of toxins as well as from the developing chronic gastritis As a result there is a delayed gastric evacuation or atony The acidity is usually reduced as well as the pepsin concentration, but the latter does not run parallel with the reduction of acidity According to our experience, as the mucous membrane becomes involved in an extensive secondary chronic gastritis, the secretion of free hydrochloric acid is rapidly diminished and a true achylia is finally produced, and at the same time the motor function of the stomach becomes impaired The gastric content at this stage reveals an absence of free hydrochloric acid and the presence of a considerable amount of mucus, much in the form of swallowed clumps

The roentgen signs are most important at this stage Lesions are rarely detected in the stomach or duodenum However, the spastic irritability of the terminal ileum, cecum, and proximal colon, as described by Brown and Sampson is observed in a large proportion of cases, indicating a definite secondary involvement of the bowel Important diagnostic information in regard to these lesions may likewise be obtained by means of barium enemas

*Course and Prognosis*.—When the dyspeptic symptoms are firmly established they rarely disappear but are likely to progress and may then in themselves account often for a rapid fatal termination. If the tuberculous affection, however, is arrested the gastric symptoms may likewise diminish, and if finally cure is brought about, a disappearance of the dyspepsia may occur.

**Treatment**.—The treatment of the gastric disturbances of pulmonary tuberculosis can only be symptomatic, inasmuch as this must necessarily be especially directed to the primary disease. Nevertheless much can be accomplished in relieving distressing symptoms and in restoring the digestive functions so that the patient will be able to consume sufficient food to aid in overcoming, as far as possible, his pulmonary disease. It cannot be denied, however, that the dyspepsia associated with pulmonary tuberculosis is less amenable to treatment than when of different origin. Diet plays an important rôle in this regard. The ideal diet for this type of patient is one which is largely restricted to meet the requirements of the bodily needs. When at rest this should consist of about 2500 to 3000 calories daily, containing approximately 60 to 90 Gm. of protein, about 200 Gm. of fat, and 100 Gm. of carbohydrates. With exercise this should be increased to about 3200 to 3500 calories containing about 125 Gm. of protein.

Inasmuch as many of these patients suffer from undernutrition, it is important that the diet should not be restricted any further than is deemed absolutely necessary and should, as far as possible, be of a high caloric type, containing the proper vitamin content. Caution, however, must be directed against overfeeding. The fattening methods commonly practiced in the dietetic management of tuberculous patients often provokes more harm than good because it throws a great burden on the already disturbed digestive tract. The food suited to the patient's condition should be given freely, heavier meals during the period of apyrexia, and lighter food in the afternoon and evening. Feeding should be moderate, though frequent, and in many instances, especially where there is secondary involvement of the bowel, food should be given in a bland form to avoid the

irritation in this region produced by the passage of roughage Milk is an important food in this affection and when it does not produce distress can be given freely It must be remembered, however, that the plan formerly practiced of forcing large amounts of milk and eggs had often disturbed the patient's digestion sufficiently so as to make it impossible afterward to again restore this function When milk disagrees, it should be modified Buttermilk or some fermented form of milk may act as a substitute Eggs can often be taken freely, but should not be forced, as they may cause indigestion Cereals, broiled tender meats, vegetables (puréed if necessary) and fruits as well as toast bread serve best as the most suitable articles of diet When there is great distress the patient must, at least for a time, be placed upon a soft diet Fatty foods often cause anorexia and should be given only with great caution The diet should be carefully arranged for the individual patient and, above all, it is important that the amount of food taken should be sufficient to maintain the general nutrition as far as this is possible

Lavage of the stomach at night will frequently relieve nausea, vomiting, and distress This is often best accomplished with the duodenal tube Drugs play an unimportant rôle in the treatment of the indigestion associated with pulmonary tuberculosis When hyperacidity exists, alkalies should be administered and when the acid is diminished or absent muriatic acid is indicated For the gastric pain and discomfort, a spirits of chloroform mixture is serviceable at times, and for the nausea and vomiting such remedies as subcarbonate of bismuth, cerium oxalate, and creosote in small doses have been found helpful Occasionally hot water taken before meals will tend to overcome nausea An ice-bag to the abdomen will also give considerable relief

We have discussed here but two affections in which gastric symptoms play a prominent rôle As we have pointed out in the beginning of this clinic, there are many others in which such secondary symptoms occur as important manifestations Space does not permit their presentation They are of unusual interest and it is hoped that they may be included in a future clinic

## CLINIC OF DR T B PUTCHER

FROM DR. WARFIELD T LONGCOPE'S CLINIC,
THE JOHNS HOPKINS HOSPITAL

### SYPHILITIC FEVER*

THE writer's interest in syphilitic fever was stimulated by Dr Osler, who frequently emphasized its importance and puzzling character, and led to the reporting of 3 cases in 1901[1] illustrating the types of fever that may occur, as well as the prompt subsidence of the fever and all subjective symptoms following the institution of iodide or iodide and mercury inunction therapy This was before the days of either the Wassermann reaction or treatment with the various arsenical preparations now in general use. Notwithstanding the intensive study and treatment of syphilis since their introduction, instances of remarkable syphilitic fever still occur, as illustrated by Case II here reported, which came under observation in 1932 Case I was observed in 1901, a week after the publication of the writer's first paper These are selected from a very considerable number of cases occurring in the Medical Wards of the Johns Hopkins Hospital

Osler and Gibson[2] in their excellent discussion of "Visceral Syphilis" devote a chapter to syphilitic fever They point out that at the end of the fifteenth and during the early part of the sixteenth centuries, when the spread of syphilis assumed epidemic proportions, the writers of the period often referred to the accompanying fever That such a fever should occur is not surprising because syphilis is an infectious disease A graphic account of it is given in the personal record of Ulrich von Hutten in his "de Guaiaci" of 1519

* The writer is indebted to Dr Warfield T Longcope, Professor of Medicine, Johns Hopkins University for the privilege of reporting the 2 cases here recorded

The earlier records lack accuracy, as clinical thermometers were not available In 1786 John Hunter says "This fever has much the appearance of rheumatic fever and after a time partakes a good deal of the nature of the hectic" Gunz (1863), a pupil of Wunderlich, the father of medical thermometry, was one of the first to study syphilitic fever by accurate methods Since then important additions to our knowledge concerning it have been made by Bristowe, Sidney Phillips, and Parkes-Weber in England, by Musser, Janeway, and Birt in the United States, by Baumler and F Klemperer in Germany, and quite recently by Strausz[3] in Hungary

Syphilis is protean in its manifestations It is still not sufficiently recognized by the profession, however, that it may give rise to protracted fever of weeks' or months' duration if its true cause has not been recognized and proper treatment instituted The most puzzling cases are those occurring in the tertiary stage of the disease, many years after the initial lesion The writer has previously recorded a case simulating typhoid fever and developing twenty-nine years after the primary sore Fortunately, at the present day, unrecognized syphilitic fever is much less common, particularly in large general hospitals, where it is a part of the routine to have a blood Wassermann test done on every patient

The febrile curve in syphilitic fever may be quite varied in its character It may present the following types

1 **Continuous Fever**—A mild continuous fever with the temperature averaging about 101 F may occur It is not infrequently the type in the fever of invasion In the tertiary stage the range may be higher and before the Widal days closely simulated typhoid There is usually some morning remission

2 **Remittent Fever**—This is probably the commonest type The temperature may reach 103 to 105 F in the evening with morning remissions toward normal This type is commonest in secondary syphilis, as shown in Case I, but may also appear in the tertiary stage

3 **Intermittent Fever**—This is the most remarkable form of all and is the type that is most likely to lead to errors in diag-

nosis With very high fever reaching, as in Case II, on one occasion 107 F and on another 108 2 F, the temperature falls for a part of the twenty four hours below the normal line Sometimes there is a combination of both the remittent and intermittent type in the same case The febrile paroxysms are not infrequently accompanied by severe chills and sweats It is the type commonly accompanying tertiary syphilis with visceral manifestations, such as gummata of the liver

Syphilitic fever may occur at various periods in the course of the disease Osler and Gibson give the following classification

1 **Preliminary Fever**—Whereas during the period of incubation there is usually no fever, yet with the malaise, loss of appetite and pallor a rise in temperature may occur A rigor may be the first sign, followed by headache, nausea, and pains in the extremities

2 **Fever of Invasion**—Statistics indicate that fever occurs in from 25 to 35 per cent of the cases of secondary syphilis, giving the so-called "fever of invasion" If temperature were taken frequently during the day it is probable that a higher percentage would show fever It may occur one to two weeks before the eruption appears According to Fournier it may be continuous, remittent, or intermittent, and is accompanied by other manifestations such as headache, malaise, and coated tongue In malarial districts it may be confused with the aestivo-autumnal type of that disease In this stage the fever may simulate typhoid, and has been referred to by Fournier as "Typhose syphilitique."

3 **Fever of the Tertiary Lesions**—Many cases of tertiary syphilis are afebrile. Gummata of the liver, spleen, lungs, and syphilitic periostitis, however, occasionally are accompanied by protracted fever of weeks' and months' duration The febrile curve may represent any one of the three types already discussed The fever is often accompanied by severe chills, sweats, headaches, anorexia, vomiting, and progressive loss in weight In this stage it often leads to errors in diagnosis, as it may occur many years after the initial lesion—twenty nine years in a case previously reported by the writer

There has been much speculation as to why fever is present in some cases and not in others Mannaberg[4] called attention to the frequency with which syphilitic fever is associated with lesions of the liver It has been suggested, when the liver is affected, that there may be a defect in the filtration mechanism between the portal and systemic blood systems Another view is that the toxins produced by the treponemata may in some instances stimulate a febrile reaction of the tissues Some hold that the thermogenic centers of the brain may be affected Finally, in rare instances, gummata may become secondarily infected with pyogenic organisms

The following 2 cases of syphilitic fever are reported to show the remarkable fever that may occur, as well as to illustrate the extraordinarily prompt cessation of the fever and relief of other symptoms on giving iodide of potassium and mercurial inunctions in one case and iodide of potassium alone in the other Case I had secondary syphilis and severe joint pains simulating rheumatic fever Case II had tertiary syphilis with features strongly resembling pleural and pulmonary tuberculosis At first there was an encysted hemorrhagic pleural effusion on the right side Later a protracted consolidation of the left lower lobe developed, which may have been gummatous in origin, as the pulmonary signs and symptoms and remarkable remittent and intermittent fever rapidly cleared up on administration of iodide of potassium No tubercle bacilli were found and a guinea-pig inoculated with the pleural fluid failed to develop tuberculous lesions

Case I —(Med No 13,172) —Primary sore eight weeks before admission, severe arthralgic pains simulating rheumatic fever, general glandular enlargement, irregular remittent fever with drenching sweats, prompt disappearance of fever and all symptoms after antisyphilitic treatment with iodides and mercurial inunctions were started

B S , male, single, aged twenty, colored, laborer, was admitted to the Medical Service of the Johns Hopkins Hospital on July 21, 1901, complaining of "rheumatism of the arms and hips," and slight cough

The family and previous history were unimportant He denied any venereal infection Subsequent investigation, however, proved this to be inaccurate It was revealed that eight weeks before admission he had had a penile chancre and a suppurating gland in the right groin

The history obtained was that five weeks before admission he developed a sore throat Five days later he complained of arthralgic pains in the right hip, followed later by similar pains in the left hip, both shoulders and the finger joints He developed a slight cough with mucoid expectoration He experienced drenching sweats but did not complain of fever His symptoms incapacitated him and he sought admission to the hospital just before midnight of July 21, 1901

The following summary of the physical findings and the course of his illness while in the hospital is abstracted from notes made by Dr R I Cole and the writer On entry he had difficulty in walking owing to pain in the hip joints There was no rash noted but he had general glandular enlargement, including the epitrochlears Various joints were painful but not swollen The lungs revealed a few moist râles at both bases There was a slight tachycardia, the pulse ranging about 100 The only feature in the heart examination was a systolic murmur at the pulmonic area which was considered of functional origin Abdominal examination was negative There was no enlargement of the liver or spleen On July 22nd the temperature, which was taken every two hours during the febrile period of his stay in the hospital, rose to 104 6 F accompanied by a drenching sweat Owing to the arthralgic pains, fever and sweating it was thought that it might be a case of rheumatic fever and he was started on 20 grains of sodium salicylate with 60 grains of potassium acetate every four hours This was continued for three days without amelioration of his pains or fever, when the treatment was discontinued The blood count showed a moderate secondary anemia, the red cells being 4,576,000, leukocytes 18,000, and hemoglobin 53 per cent. Repeated examinations of the fresh blood for malarial parasites yielded negative results On July 23rd Dr Cole noted an indurated almost completely

healed scar behind the corona of the glans penis on the right side, and there was a healed scar of a recent suppurated gland in the right groin

The febrile course in the patient is given in Fig 196, where only the highest and lowest daily temperatures are recorded Each day there was a marked paroxysm of fever accompanied by severe sweats On July 25th the writer made the following note "The patient has had profuse sweats since admission Considering that he has evidences of a recent sore on his penis

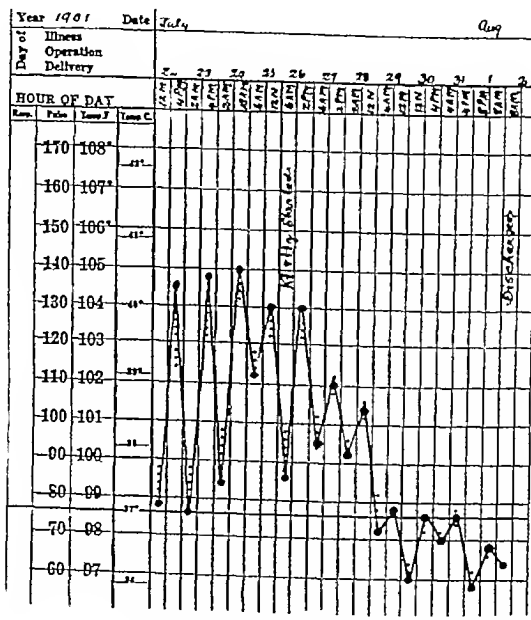


Fig 196 —Highest and lowest daily temperatures (Illustrating Case I)

and a well-marked general glandular enlargement syphilitic fever has to be considered, and antisyphilitic treatment is to be started, consisting of iodide of potassium in increasing doses, together with mercurial inunctions "

Accordingly, as salicylates had been ineffectual, on July 26th the patient was started on 1 Gm (15 grains) of iodide of potassium three times daily after meals, to be increased 0 3 Gm (5 grains) to the dose every other day, as well as daily inunctions of 4 Gm (1 drachm) of mercury ointment As the chart shows,

there was a very prompt reduction of the fever on this treatment On July 26th the temperature reached 104 F The following day it fell to 102 F , the next day to 101 4 F and on July 29th the fourth day after antisyphilitic therapy was started the temperature returned to normal and remained normal from then on The cessation of the fever was accompanied by a disappearance of his joint pains and he was able to leave the hospital free of symptoms on August 2nd thirteen days after admission

*Discussion* —This case illustrates four points (1) The type of remittent fever that may occur in the secondary stage of syphilis (2) With the severe arthralgic pains the simultation of rheumatic fever (3) The importance of careful search for evidences of a primary Hunterian sore The case occurred before the Wassermann test had been discovered (4) The prompt cessation of the fever, arthralgic pains, and all other subjective symptoms on the institution of iodide and mercurial therapy Salvarsan and other arsenical preparations were then not available

Case II —(Unit History No 19,307) —Syphilitic fever of remittent and intermittent type, reaching on one occasion 107 F and on another 108 2 F , in a colored woman with a syphilitic husband Patient gave birth to two full term stillborn children and had a syphilitic placenta Positive Wassermann Chills, sweats, nausea, and vomiting Hemorrhagic pleural effusion on left side and later signs of consolidation of left lower lobe resembling tuberculosis Prompt disappearance of fever and lung signs and striking general improvement after starting iodide of potassium

I C B , female, colored, aged twenty six, was admitted to Osler III of the Johns Hopkins Hospital, on June 21, 1932, complaining of weakness, vertigo, severe sweats, cough, and expectoration Her mother had had numerous miscarriages Husband died at the Johns Hopkins Hospital on October 21, 1931, of syphilis, syphilitic aortitis and aortic insufficiency, confirmed at autopsy He had a positive Wassermann Patient had been married to this man nine years No history of tuberculosis in the family

Patient had been admitted to the Johns Hopkins Obstetrical Service five times In 1923 and 1924 gave birth to full-term, healthy children In 1928 was delivered of a full-term, stillborn child In 1929 of a full-term, stillborn, macerated baby On this admission her blood Wassermann was positive and the placenta syphilitic After discharge she attended the Out-Patient Syphilitic Clinic, where she received nine intravenous arsphenamine injections and her blood Wassermann became negative In March, 1930, she gave birth in the Obstetrical Ward to a full-term, apparently healthy baby

After the birth of this fifth child she was instructed, on leaving the hospital, to continue treatments at the Out-Patient Syphilitic Clinic On April 25, 1930, she was given an injection of 0 2 Gm of bismuth She failed to return for other treatments and the Social Service Department was unable to locate her, as she had moved from her former address

Patient did not come under observation again until March 27, 1932, when she was admitted to Osler III complaining of severe pain in the lower right chest, with cough and mucopurulent expectoration She had a pleuritic friction rub and later signs of fluid developed Two aspirations yielded 40 and 10 cc of hemorrhagic exudate *x*-Rays revealed an encysted exudate Fluid negative on culture and no tubercle bacilli found Guinea-pig inoculation revealed no tuberculous lesion at the end of six weeks Temperature range was from 99 to 101 8 F during her stay in the hospital Discharged on April 13th with a diagnosis of "Latent syphilis, acute pleurisy of undetermined cause" On the possibility that her pleurisy might be tuberculous she was sent to the Colored Tuberculosis Sanitarium at Henryton on May 4th Remained there only three weeks, leaving against advice

She was readmitted to Osler III on June 21, 1932 Three weeks previously had had a rather profuse uterine hemorrhage Two weeks before entry more acute manifestations developed with fever, chills, sweats, nausea, vomiting, vertigo and fainting attacks, and cough with mucoid expectoration On examination she was obviously an ill woman On the day of entry the tem-

perature rose to 107 F There were no enlarged glands and no nodes on the bones Dr Bedell's note on the lungs on admission was as follows "Thin chest wall Right side moves more than left Percussion note slightly impaired in the left posterior axillary region and at the left base Breath sounds a little distant at right base A number of crepitant râles present at left base, left axillary region and anteriorly to the left border of the heart in the fourth and fifth interspaces No tubular breathing made out Whispered voice sounds normally transmitted" On the day of entry the blood count was as follows Red cells 2,110,000, leukocytes, 18,600, hemoglobin, 55 per cent, polymorphonuclears, 88 per cent Chest *x* rays were taken on June 22nd and following is Dr Waters' report "Pleurisy at right base has entirely disappeared There is now infiltration in the left lower lobe that looks to be in the lung and not in the pleura"

On June 26th, Dr Tillet noted that there were daily chills and sweats He found that the dulness had increased at the left base and that there were now numerous coarse moist râles over the lower lobe. The breath sounds were slightly tubular and the sputum blood tinged On June 27th another *x* ray of the lungs was taken, the report being as follows "Pneumonic consolidation at left base Obliteration of the right costophrenic angle probably due to pleurisy" That night the temperature rose to the remarkable height of 108 2 F

During the patient's stay in the hospital seven chest *x*-rays were taken On July 7th and 22nd Dr Waters and Dr Pierson reported evidences suggestive of breaking down of lung tissue in the left lower lobe

The sputum throughout her illness was abundant, ranging from 100 to 200 cc daily It was frequently examined bacteriologically No tubercle bacilli were ever found Sputum cultures showed an hemolytic staphylococcus aureus Stained smears from the sputum showed a gram positive diplococcus and a few spirochetes and fusiform bacilli

Repeated blood cultures were negative. On June 23rd the blood Wassermann was positive by the flocculation method A careful pelvic examination was reported to be entirely negative

The clinical picture was dominated by the respiratory features with cough, abundant expectoration, and a remarkable fever accompanied frequently with chills and sweats While on active duty on Osler III in July the writer saw this patient for the first time on July 6th when the following note was made "Lungs, right, essentially clear on percussion and auscultation Left, moderate impairment of the percussion note over the submammary, lower axillary, and subscapular regions No definite friction rub Vocal fremitus, vocal resonance, and breath sounds

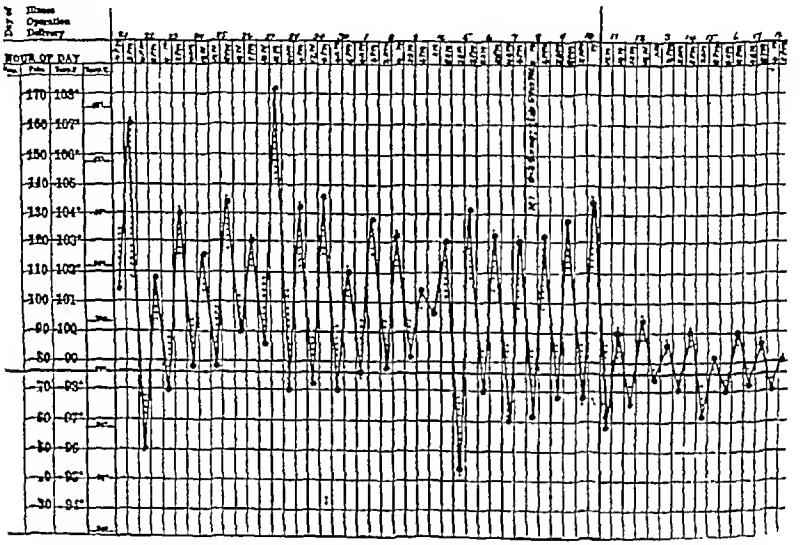

Fig 197 —Highest and lowest daily temperatures (Illustrating Case II)

diminished over the lower lobe No definite tubular breathing Liver and spleen not felt "

The case was discussed with the House Staff, and, as the patient obviously had syphilis, the possibility that the patient was suffering from tertiary syphilitic fever was considered Osler's axiom concerning obscure fevers "When in doubt give potassium iodide" was emphasized Accordingly, on July 8th, it was recommended that the patient be given 1 Gm (15 grains) of potassium iodide three times daily after meals, to be increased by 0 1 Gm (1 5 grains) to the dose daily Owing to a misunderstanding, only 0 2 Gm (3 grains) three times daily was begun

on July 8th and increased by 0 1 Gm (1 5 grains) to the dose daily The remarkable effect of the drug on the temperature is shown in Fig 197 For the first three days there was no effect on the fever the highest temperature on July 10th reaching 104 4 F On July 11th, the fourth day after iodides were started there was a striking subsidence in the fever the temperature only reaching 100 F With very slight oscillations the temperature reached normal on July 18th ten days after the drug was started

The improvement in the patient's general condition was most striking She rapidly regained her appetite The cough and expectoration progressively subsided and the dulness and other signs at the left base gradually cleared up and had practically disappeared when she was discharged from the hospital on August 19th feeling perfectly well Her weight steadily increased From July 17th, when she was first strong enough to be weighed, to August 14th, she had gained 16 pounds The last *x* ray before leaving the hospital was taken on August 16th and was interpreted by Dr Pierson as follows, "Area of partial consolidation in lower lobe of left lung, associated with thickened pleura' There had been a striking diminution in the degree of density and the changes were mainly in the form of irregular lines of fibrous thickening

On leaving the hospital on August 19th she was referred to the Dispensary Syphilitic Clinic, where up to November 17th she had been given five intravenous injections of 0 3 Gm of arsphenamine and three intramuscular injections of 0 3 Gm of bismuth Blood Wassermann negative on September 29th and October 13th

She was seen personally on December 16th Subjectively, she had been perfectly well since leaving the hospital Temperature 98 6 F No cough Weight 125 pounds, a gain of 21 pounds since July 17th

On December 16th another *x* ray of the chest was taken, Dr Pierson's interpretation being as follows "Moderate amount of fibrosis of left lower lobe, does not appear to be much change since last examination"

*Discussion* —This patient was a proved syphilitic. Her blood

Wassermann was positive Her husband had died in the hospital of syphilis, syphilitic aortitis, and aortic insufficiency proved at necropsy She had given birth to two stillborn children and had a syphilitic placenta The prompt cessation of the remarkable fever and striking general improvement on instituting treatment with iodide of potassium leaves no doubt but that she was suffering from tertiary syphilitic fever It is rather remarkable that the fever subsided so promptly even on such small doses of the drug With all the various arsenical preparations now so commonly used in the treatment of syphilis, the case illustrates admirably the efficiency of iodide of potassium in the treatment of tertiary syphilitic fever It also emphasizes the force of Osler's oft-repeated axiom in the case of obscure fevers, "When in doubt give KI," as will be demonstrated by a glance at the temperature curve in Chart 2

With the exception of the remarkable fever, with chills and sweats, the pulmonary features in this case dominated the picture During the admission preceding the last one she had an encysted right-sided, hemorrhagic pleural effusion which was proved to be nontuberculous by guinea-pig inoculation, although she was later sent to a sanitarium for tuberculous patients as a suspect On the last admission the question naturally arose as to whether the fever was dependent upon the consolidation of the lower left lobe and there was considerable speculation as to the nature of this pulmonary lesion It is always rather venturesome to make a diagnosis of lung syphilis without autopsy proof, the finding of treponemata in the tissues, or obtaining positive proof by animal inoculation The prompt cessation of the cough and expectoration and progressive clearing up of the lung signs on the administration of potassium iodide, however, renders it quite probable that the patient had a gummatous pneumonia of the lower left lobe The areas in this lobe interpreted as possible cavitation in one of the *x*-ray films may have been due to caseation and breaking down of syphilitic lung tissue The question naturally arises as to whether or not the encysted, hemorrhagic pleurisy with effusion on the right side on the previous admission may have been of syphilitic origin

Buchanan,[5] of Liverpool, in 1907, reported a case with symptoms and pulmonary signs very similar to the present case in a syphilitic man, aged forty eight, who complained of cough, expectoration, dyspnea, fever, night sweats and emaciation Prompt general improvement and disappearance of the lung signs followed the administration of iodide of potassium No tubercle bacilli were found The progress in the clearing up of the lung condition was followed by *x* ray studies

In our case there was unquestioned syphilitic fever as demonstrated by the therapeutic test Whether it was dependent upon visceral syphilis of the pulmonary type may be left an open question It is the firm conviction of the writer, however, that the patient had pulmonary syphilis One of the best discussions of lung syphilis is by Osler and Gibson[6] in their article on "Visceral Syphilis"

Diagnosis —In the diagnosis of syphilitic fever the first and important essential is to always keep in mind that obscure fevers may be of syphilitic origin In the "fever of invasion" errors in diagnosis will be less likely, although they occur, if inquiry is made concerning the occurrence of a recent primary sore and if the patient is carefully examined for mucous patches general glandular enlargement, and the secondary skin eruption A positive Wassermann would be strongly confirmative evidence Even in this stage, as in Case I, the joint pains may strongly resemble rheumatic fever

It is in tertiary syphilis, many years after the initial lesion that error in the diagnosis of the fever is most likely to occur The discovery of evidences of gummata of the liver or spleen with enlargement of these organs, of obscure lung lesions, and, finally, of tender periosteal nodes on the clavicles or other long bones should arouse strong suspicion

The diseases with which the remarkable continuous remittent or intermittent fever of tertiary syphilis has been most frequently mistaken are

1 *Rheumatic Fever* —Syphilitic nodes adjacent to joints may cause periarticular enlargement with severe pain, and with an accompanying fever and sometimes sweats may be regarded as

one of acute rheumatic fever Osler cites such a case in a girl of nineteen The elbows, one wrist, and both knees were affected There was slight fever The correct diagnosis was established by finding nodes on the clavicles and after a more careful examination of the joints

2 *Malaria* —The literature contains records in which the chills, fever, and sweats have closely resembled and been mistaken for malaria The writer has previously reported such a case in a physician, who thought he had malaria His blood was negative for parasites Inquiry revealed he had contracted a syphilitic infection twenty-nine years before The fever and chills promptly subsided on the administration of iodides A remarkable case was reported by Sidney Phillips[7] in a woman who had had intermittent chills, fever, and sweats occurring every other day for a period of eight months Quinine was ineffectual but there was prompt relief after administration of iodide of potassium

3 *Typhoid Fever* —Cases of syphilitic fever mistaken for typhoid are rather uncommon but do occur Osler and Gibson state that of 3076 cases admitted to the London fever hospitals wrongly certified as having typhoid fever only 10 were subsequently proved to have syphilis J D Rolleston[8] has reported in detail 2 cases of syphilitic fever which simulated typhoid The writer has previously reported a case, occurring before the days of the Widal test, which was at first suspected of being typhoid fever The patient, aged thirty-nine years, had had a continuous fever for three weeks before admission After admission to the Johns Hopkins Hospital the temperature chart showed a remittent and intermittent fever from August 8th until September 16th He had a furred tongue and an enlarged spleen Blood examinations showed no malarial parasites On September 12th Dr W S Thayer noticed the presence of thickening of the clavicles from old nodes Suspicion was aroused and examination revealed a definite scar on the glans penis and the patient admitted infection Potassium iodide was at once started and by September 16th his temperature was normal There was no further rise in temperature and he was discharged on October 3rd perfectly well

4 *Tuberculosis*.—Syphilitic fever has been mistaken more frequently for pulmonary tuberculosis than for either malaria or typhoid. The simulation is illustrated by Case II. Many writers have referred to it. It is in the form in which there are sweats, irregular hectic fever, loss of weight and slight cough, that tuberculosis is suspected. Sergent[9] has discussed the relationship. Janeway[10] in 1898 drew special attention to the prevalence of this error in diagnosis. He reported 6 cases of syphilitic fever that had been interpreted and treated as tuberculosis. The cases subsequently came under his personal observation. Four had been sent to sanitaria for tuberculous patients without benefit. Careful examination and inquiry into the history of each case led to the diagnosis of syphilis, with prompt disappearance of the fever and restoration to health after the commencement of antisyphilitic treatment. Morgan[11] reported a case of syphilitic fever of intermittent type in which acute miliary tuberculosis was for a considerable time suspected. The absence of tubercle bacilli from the sputum, together with the securing of a syphilitic history, led to the administration of potassium iodide with prompt cessation of the fever and all other symptoms.

Pulmonary hemorrhage may complicate syphilis of the lung and strongly simulate pulmonary tuberculosis. Remsen,[1] in 1903, reported a case of syphilis of the lung that was admitted to the Johns Hopkins Hospital who died suddenly from a severe hemoptysis. At autopsy there was found just below the left apex a caseous mass surrounded by scar tissue. The right lower lobe was almost entirely solid with caseous masses separated by strands of connective tissue. In the middle there was a cavity, 3.5 cm. in diameter filled with blood, which opened into a bronchus, and which had eroded directly into a branch of the pulmonary artery. No tubercles nor tubercle bacilli were found. In commenting on this case Osler and Gibson say, "This case shows the existence of progressive destructive disease, a true syphilitic phthisis."

5 *Septic Infection*.—The remittent and intermittent types of syphilitic fever, particularly when accompanied by chills, fever

and sweats, may closely simulate that accompanying a localized abscess or that associated with a general septicemia It may resemble a bacterial endocarditis with a blood stream infection Negative heart examinations and repeated negative blood cultures should rule out an endocarditis Careful search for focal infection should always be made The fever and chills may also be simulated by an obscure, deep-seated phlebitis

**Treatment**—In the diagnosis of syphilitic fever the therapeutic test is the most conclusive Before the days of the Wassermann reaction this was much more important than it is today When no adequate cause for the fever has been found much valuable time and suffering may be saved by the early institution of some form of antisyphilitic treatment There are few more satisfactory experiences in the treatment of disease than the prompt cessation of the fever within a very few days and the rapid amelioration of all subjective symptoms when adequate antisyphilitic treatment is started in cases of syphilitic fever

Today the natural tendency is begin at once with intravenous injections of one of the various arsenical preparations now so commonly in use The results are, to be sure, most gratifying But they are not necessary It is not sufficiently recognized by the profession today that as prompt and satisfactory results are obtained by the administration of iodide of potassium alone or in combination with mercurial inunctions, particularly in the fever of tertiary syphilis The writer cannot too strongly emphasize the importance of Osler's axiom, "When in doubt give KI" The satisfactory results are well illustrated in the 2 cases here reported

In the administration of iodide of potassium a very good plan is to begin with 1 Gm (15 grains) three times daily after meals, increasing 0 3 Gm (5 grains) to the dose every other day until a total of at least 6 to 10 Gm (90–150 grains) daily is taken Syphilitics have a remarkable tolerance for iodides With this drug alone syphilitic fever will almost invariably show a striking drop in the temperature within four or five days With the iodides, daily inunctions of 4 Gm (60 grains) of mercury ointment may also be administered, guarding of course

against salivation Even though satisfactory initial results are obtained by the use of iodides and mercury, it is most important that their use should be followed later by repeated courses of intravenous injections of one of the arsenical preparations, possibly alternating with intramuscular injections of bismuth, over a period of months or years to rid the patient of his syphilitic infection and thus prevent a recurrence of the fever and other manifestations of the disease The Wassermann tests on the blood and spinal fluid will determine how long the treatments should be continued

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## CLINIC OF DR THOMAS R BROWN

JOHNS HOPKINS HOSPITAL

### CHRONIC DIARRHEAS

I THOUGHT it might be interesting today to present a group of cases having one symptom chronic diarrhea in common although there is a striking difference in the etiologic factors in the different cases

It is surprising how frequently one finds the diagnosis of "constipation" or "diarrhea" made yet we must know how perfectly unscientific such a diagnosis is, it can never be more than a symptomatic diagnosis Appreciation of the underlying causes is essential as our diagnosis should be based not on symptomatology but on etiology and pathology because by no other means can a proper therapy be instituted

Gastrogenous Diarrheas —The first 2 cases I wish to present together are interesting because their symptoms were entirely intestinal, their cause entirely gastric Two young men—one an Austrian, one an Irishman—both high strung both extremely well physically, and in each of whom after a violent shock diarrhea developed—a diarrhea intractable to the ordinary methods of treatment, dietetic astringents rectal irrigations, etc , and in both of whom the stomach had never been considered a potential factor because there was never a gastric symptom In each of these cases the symptoms had lasted several years before the patient was seen and in each case the physical examination was strikingly negative The stool showed no occult blood and no parasites The test meal showed a gastric achlorhydria The administration of small doses of dilute hydrochloric acid, from 15 to 25 drops, with each of the three meals brought instantaneous relief in each case, but in each case the therapy had to be continued for over a year before there was a return of

acid secretion in the stomach, coincident with which the diarrhea disappeared without the use of further therapy

These cases are interesting because they represent the psychogenic factor in gastric secretion, because they make one realize how long an achylia of this origin may last after the block, presumably the vagal block, has been established, and last of all because they accentuate the importance of making gastric analyses in each case of diarrhea without obvious cause, especially those in nervous individuals following shock

The fact that small doses of dilute hydrochloric acid give as complete relief as extremely large doses—several hundred drops as used in certain of the German clinics—makes one realize that it is not the substitution of the lacking acid that plays the fundamental rôle, but some rôle that acid, even in small amounts, plays in controlling the normal motor mechanism of the intestinal tract

In our experience this is not a negligible group of cases, but a larger group of this so-called "gastrogenous type" appears in very old people where the teeth are defective or deficient or absent, again where there are no gastric, only intestinal symptoms, and again where small doses of hydrochloric acid give complete relief, but in this group of cases the acid has to be given indefinitely as a rule because there is no return of acid in the gastric secretion They probably represent a definite senile atrophic gastritis with complete disappearance of glandular activity

**Pancreatogenous Diarrheas**—A much smaller but equally interesting group is that in which disturbances in pancreatic secretion is the cause of the diarrhea Let me give a case in point The patient was a woman who, a number of years ago after an acute attack of gallstone colic, was operated upon and 18 gallstones removed and the gallbladder drained for a short period of time A few weeks later she developed a diarrhea and the test meal showed a gastric achylia, which is not at all uncommon in biliary tract disease, and hydrochloric acid therapy was absolutely successful in controlling the condition This finally could be discontinued as she had a return of normal acid

secretion Fourteen years after the first operation the patient had a recurrent attack of gallstone colic so severe that she was operated upon again The gallbladder was found filled with small stones and was removed Shortly afterwards she again developed a diarrhea but of a very different type The stool was a typically butter like stool The estimation of the pancreatic ferments showed absence of diastase and trypsin and the patient got relief from the administration of pancreatic extract in large amounts, though this did not have to be kept up for a long period of time as the stools regained their normal character in a few weeks and the diarrhea ceased

The case is interesting because it probably explains the diarrhea that is present after a small proportion of cholecystectomies it is probably pancreatogenous, and in our case at least it was relieved by pancreatic ferments That the pancreatic trouble was purely functional was shown not only by the rapid return of normal stools and the reappearance of pancreatic ferments in the stool, but by the fact that at a subsequent operation made a few months later for adhesions around the gallduct, the pancreas was found to be absolutely normal, just as it had been found at the time of the second operation

This is a small group of cases, but a very interesting one

**Diarrhea and Hyperthyroidism** —We have reported in the past few years a considerable number of cases of unrecognized hypothyroidism, usually in women of the late forties, usually obese, in which striking constipation has been the only symptom and in which the condition can only be diagnosed by basal metabolic readings and by the effect of thyroid therapy, *forme frustes*, as it were, of hypothyroidism where the only symptoms that seemed to be evident were intractable sluggishness of the gut

The reverse of the picture—where intractable diarrhea—is the only, or at least the main, symptom of unrecognized hyperthyroidism, is also met with but much more rarely in our experience

A case in point is a man of sixty five years of age whose only complaint was diarrhea He was very active mentally and in

tellectually an excessively hard worker His complaint was diarrhea of the intermittent character but quite intractable to ordinary treatment which had lasted over three months He had been carefully studied and the case diagnosed as a colitis, but the treatment, dietetic and medicinal, had been utterly ineffective There had been a moderate loss of weight, no obvious fever, no gastric disturbance whatsoever, no pain with the diarrhea, there had always been a little tendency to loose movements throughout his entire life

The physical examination was singularly negative He had a slight tremor of the hands, a slight tachycardia with no organic lesion, a normal blood pressure, 152/72, the thyroid was not palpable, the knee jerks were exaggerated, and there were many evidences of fatigue

The test meal was essentially normal—free acid 20, total acid 33 The stool was absolutely normal except it was loose, there was no evidence of any undigested foodstuffs The hemoglobin was normal

The x-ray examination of the gastro-intestinal tract, made in Washington as well as in Baltimore, simply showed a very spastic irritable colon with no defect and no absence of haustration, while the sigmoidoscopical examination was completely negative

The basal metabolic test, however, gave the clue to the solution, it was plus 42 per cent

The case was therefore regarded as a probable hyperthyroidism apparently with exacerbations of overactivity of the thyroid from time to time, when presumably the diarrhea appeared Under rest, Lugol's, general upbuilding treatment, the patient did extremely well He gained 11 pounds, became much less nervous, his diarrhea ceased, his basal reading dropped to plus 11 5 per cent, his pulse was normal and this improvement has continued although occasionally he has to rest and take Lugol's for a short period of time

The preceding group of cases is interesting in calling attention to certain forms of diarrhea in which the motor mechanism seems to be affected by various agencies, one, the absence of

hydrochloric acid in the stomach, though this cannot be the only factor because there are many achylias without diarrhea, second where functional pancreatic disturbances are the basic cause and third, where unrecognized overactivity of the thyroid gland manifests itself practically exclusively in the intestinal sphere

In all of these cases, with the exception of the presence some times of undigested food due to hypermotility and, in the pancreatic group, the fatty stools, we have no absolute clue to the cause of the condition except by study elsewhere

To this group should probably be added the purely nervous diarrheas with no evidence of hyperthyroidism or achlorhydria—the tabetic diarrheas and the reflex diarrheas due not to disturbances in the gastro-intestinal tract, but to lesions elsewhere

Between this group and the following cases which I shall present falls the large number of cases of enterocolitis with chronic diarrhea due to catarrhal conditions of the tract associated with various forms of traumata, food, etc —the so-called "entero colitides" Perhaps one of the most interesting of these are those cases of diarrhea due to an enterocolitis following gastro-enterostomy, obviously due to irritation of the tract by improperly chymified food and quite obviously suggesting the importance of very careful postoperative dietetic care for a considerable time after gastro-enterostomy until the intestinal tract has been reeducated, as it were, to take care of food which has not had the usual chemical and physical changes met with in normal gastric digestion

The second large group are chronic diarrheas in which there is definite evidence of ulceration These cases are of even greater importance because they are not only of greater severity and are more difficult to treat, but it is even more essential that the underlying pathology be appreciated as early as possible because in certain cases the only effective therapy is based on early, or relatively early diagnosis

**False Diarrheas in Malignancies of the Colon**—I will give in brief the history of a case of this type which I saw recently A man sixty years of age, with a singularly negative family and past history, with good habits of eating and drinking and no

digestive disturbance of any kind until one year before I saw him, when, after a severe mental strain, he began to have diarrhea After a short time the stool showed microscopically blood and pus For the preceding year the stools had been in number from twelve to twenty-five in twenty-four hours The patient had had constant pain over the transverse colon, his appetite, if anything, was increased, but his diet had been very much restricted by the various physicians he had seen He had a low fever but recently there had been no obvious blood in the stool —only mucus in considerable amounts He had been treated as a case of chronic diarrhea and it had been suspected that the initial symptoms were those of chronic dysentery

He had lost a very considerable amount of weight and the physical examination very definitely confirmed this fact He was markedly anemic, but the only thing of striking moment was a hard nodular mass palpable in the lower left quadrant and above this a line of masses running up to the splenic flexure, which were quite obviously fecal tumors

The rectal examination was negative The sigmoidoscopical examination showed no evidence of organic lesion, although it was impossible to get the instrument beyond 16 cm Blood and mucus were seen trickling down from above this area and the microscopical examination showed many red blood cells and a moderate number of pus cells with a moderate amount of mucus A very careful study by the ligroin method failed to show tubercle bacilli The blood showed 58 per cent of hemoglobin, 3,970,000 reds, and a white count of 9000 with 70 per cent of neutrophils

Studying the bowel by the barium enema fluoroscopically we were unable to get any barium to show beyond the upper rectum There seemed to be a definite obstruction at this point

Diagnosis was of course a malignant growth at the rectosigmoidal juncture producing partial obstruction and this was confirmed by operation Unfortunately the growth had become adherent to the bladder and to the posterior tissues and a colostomy was all that could be done to relieve the obstructive symptoms

The case is interesting because it illustrates the fact that in certain cases of malignant growth of the large bowel, the ulcerative irritative phenomena may be so marked, the obstructive phenomena so slight that the case may be regarded as a diarrhea and treated accordingly, when the true nature of the condition, partial obstruction with ulceration, is not recognized and valuable time is lost before the correct diagnosis is established

It accentuates the point that all change in intestinal habit coming on in persons, especially those in the later life and in people who have had no digestive symptoms previously, should be studied with the most meticulous care—stool studies, sigmoidoscopical examinations, very careful palpation in the hot bath if the abdomen is difficult to palpate, and very careful fluoroscopical studies with the barium enema—because by these means only can the diagnosis be made at a time when resection and cure is possible

**Nonspecific Ulcerative Colitis**—The next group of cases represents a condition which is becoming unquestionably more prevalent and more interesting—chronic diarrheas due to the so-called "nonspecific ulcerative colitis", an ulcerative lesion of the colon, not tuberculous, not malignant, not parasitic, not due to bacillary or amebic dysentery, cases in which many if not most observers still feel that the primary cause has not been determined, although some believe that the diplococcus of Bargen is the fundamental etiologic factor Many other views as to its etiology have been expressed, that it is due to certain other micro-organisms, virulent colon bacilli, streptococci, etc., that it is the aftermath of a bacillary dysentery as suggested by Hurst, that it represents the expression of a diet deficient in the vitamins as suggested by Larrimore, that it has fundamentally a psychogenic basis as suggested by a number of recent observers based on the fact that many of these cases are found in young neurotic individuals with all the stigmata of autonomic imbalance, that it represents some disturbance in the absorptive power of the lower gut or some factor, possibly metabolic, that causes a lowered resistance of the gut to ordinary intestinal flora

Frankly, no explanation so far given seems satisfactory to me and for that reason I still think the name "nonspecific ulcerative colitis" is the best one to use

The first case was in an extremely strong, absolutely healthy man, who without rhyme or reason, developed an ordinary painless diarrhea and was treated as such for about a month before we saw him The stool showed a large amount of pus, very positive occult blood, and the sigmoidoscopical examination showed a typical picture of a nonspecific ulcerative colitis, that is, edema, hyperemia friability and small punctate erosions and ulcerations

He responded successfully to no treatment, rest, rectal installations of various kinds, bland powders, Lugol's solution, high vitamin, high caloric low residue diet, and became progressively worse, a few weeks later developing recurrent hemorrhages requiring several blood transfusions Ileostomy was performed and after the operation he had five or six transfusions as his postoperative course was at first very stormy, but later he got progressively better and left the hospital with a well-fitting cup over the ileostomy, and went about his work Two years later the stool, sigmoidoscopical and fluoroscopical studies showed a normal intestine, the ileostomy was closed and he has been well and symptom-free ever since

The second case illustrates the apparent rôle that the psychic factor plays in certain cases This case was that of a very high-strung, emotional young woman She gave no history of any previous disease of special moment except that fourteen years before she had had a similar attack of diarrhea, which was definitely diagnosed as ulcerative colitis For this she had been in the hospital for several months without improvement, in fact, she had made no improvement at all until she had had a number of teeth removed, and it was questionable whether many of them were appreciably diseased However, after their removal the trouble gradually cleared up and she had had no symptoms or signs of the condition until shortly before being seen by us

Fourteen years later and six months before she was seen by us, after a severe shock there was a recurrence of the entire symp-

tom complex, painless diarrhea, blood and pus in the stool, progressive loss of weight and an absolute inability to get relief from any of the usual measures When seen by us she had the classical picture—a lack of haustration in the sigmoid, the lead pipe feel of that portion of the gut to palpation, pus and blood in the stool, a very spastic rectum with an edematous and friable mucosa with a few pin point ulcers

Under rest, bland powders, high vitamin low residue diet forced feeding, sunshine and upbuilding treatment, the patient made a steady progress and finally became clinically well, only to have a recurrence of her symptoms three months later when she got temporary relief, at least, under similar therapy

In this instance various other things were tried as the case was rather intractable Parathormone, calcium gluconate Aolan, in other words, nonspecific protein shock (and in this connection in certain cases we have also tried pneumococcus serum, dead typhoid and colon bacilli, without incidentally ever convincing ourselves that any of them produced any appreciably beneficial effect), but in this case as in many others, we were forced to conclude that general upbuilding treatment, rest, sunshine, and freedom from strain played a larger rôle than any of the highly recommended "specific' therapeutic agencies which have been suggested for this condition

The third case was a young man of twenty four years, who had suffered for five years with diarrhea, sometimes better, sometimes worse, interspersed with a number of hemorrhages, never very large, and who had had all the usual treatment diet, Bland powders, nonspecific protein shock, serum and vaccines at the Mayo Clinic, and who had become better and worse, but was never well

His previous history was perfectly normal, he had never been sick previous to 1927 when his condition started As in most of these cases, the diarrhea was painless. The diagnosis was confirmed by very careful sigmoidoscopical, radiographical, and stool studies

The patient was anemic, and as in many other cases was materially helped by very large doses of iron (as a rule using Blaud's

pills or reduced iron) and by repeated small transfusions, which in our experience are invaluable in the treatment of this group of cases, especially of course in those with marked anemia or in the so-called "hemorrhagic type" with repeated hemorrhages

Under careful hospital treatment in which rest, small transfusions, forced feedings, and sunshine played the major rôle, he gained weight and improved very materially, but from stool studies and palpation of the sigmoid, from sigmoidoscopical investigation and barium enema studies, it was quite obvious that the underlying condition still existed This was definitely shown from the fact that when he left the hospital all his symptoms returned, so that when he came back to us again ileostomy was performed and after a rather stormy early convalescence (incidentally quite usual after ileostomies in this type of case) he became progressively better and is now comfortable and clinically quite well How long the ileostomy will have to be kept open is a problem We have had cases in which successful closure was made in eighteen months or two years, and one case in which closure after six months was absolutely successful

Some of these ileostomies of course must be regarded as permanent, but in our experience, at least, this is not so in a fair proportion of cases

As to the choice of operation, in our experience ileostomy is by all odds the most effective Appendicostomy is not necessary in the milder cases and is not effective in the severer cases, and ileosigmoidostomy can only be done in a very small proportion of cases (from 5–15 per cent), where the site of the disease is mainly confined to the cecum and ascending colon, and not, as is the case in the vast majority of cases, primarily localized in rectum and sigmoid

The next case is that of a young girl, high strung, very clever, always rather frail, who came to us after a history of four years of classical ulcerative colitis, and who had been treated by many men and many methods, but without success In her case we felt perhaps more convinced than in any of the others of the inefficacy of most of the highly recommended procedures, and we were absolutely convinced that with her rest, sunshine, appro-

priate diet and freedom from nervous strain played the major rôle in the very marked improvement which she made She gained 20 pounds, was able to go to school had only one or two movements a day and the condition of her blood was very much better although she always had a definite secondary anemia with a hemoglobin around 70 per cent and the red corpuscles were only a little over 4,000,000 The stool always showed occult blood and a few pus cells

The interesting thing in her case was after two years of comparative freedom from active symptoms, she developed definite symptoms of lower intestinal obstruction and palpation showed a marked hypertrophy of the sigmoid The obstruction was so nearly complete that operation had to be performed and an enormously hypertrophied sigmoid filled with multiple small abscesses was removed After a long convalescence the patient became progressively better though she still has a small fecal fistula

This case is interesting because of the relative rarity of obstructive signs and symptoms in this condition, a thing hard to explain because one would think that with such extensive ulceration, with such extensive involvement of the layers of the gut as demonstrated by *x* ray study and palpation, stricture would be very common

The last case is one in which the symptoms from the very first were almost entirely confined to lower sigmoid and rectum As in so many of these cases apparent spontaneous recovery occurred from time to time, only to be followed by recurrences without apparent cause Careful sigmoidoscopical and *x* ray studies showed that the pathology was almost entirely confined to lower sigmoid and rectum, while the sigmoidoscopical studies showed an enormous number of small polyps and granulomata in these areas, interesting because certain cases of multiple polyps owe their origin to an antecedent ulcerative colitis In 2 cases right sided malignant degeneration of one of these polyps had taken place, though as a rule malignancy is not commonly met with as a late complication of nonspecific ulcerative colitis

In this case, intravenous injection of tartar emetic seemed to have given very definite temporary relief, but the result was not permanent and both the symptoms and the granulomata reappeared

This group of cases seems to me very interesting because it makes one realize the variations which an ulcerative colitis may play in its clinical course, here a mild painless diarrhea and a purely local problem, here a picture with a rapid downward course often interspersed with large hemorrhages, here where the metastatic phenomena of erythema nodosum, arthritis, evidences of myocardial change are quite marked, or here where the condition begins and ends as a local process

I present these cases of chronic diarrheas to call attention primarily to the importance of investigating the cause in each individual case, to demonstrate how important it is to make the most thorough analyses of history, the most careful examinations and the most intensive technical studies in these cases, because without this the primary cause in many of these cases will not be determined and the proper therapy cannot be instituted In both groups of cases, especially the latter group, no one can be too careful in the special examination of the large bowel itself—repeated stool studies on a meat-free diet, proctoscopical and sigmoidoscopical examination, very careful x-ray studies, preferably fluoroscopical with barium enema, and very careful palpation of the abdomen

CLINIC OF DRS M C PINCOFFS AND C C SHAW

FROM THE DEPARTMENTS OF MEDICINE AND PATHOLOGY
UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE

## THE EASTERN TYPE OF ROCKY MOUNTAIN SPOTTED FEVER. REPORT OF A CASE WITH DEMONSTRATION OF RICKETTSIAE

THE cities of the Eastern coast of the United States were periodically afflicted by epidemic typhus during the last century but no major epidemic of this disease has been seen in Baltimore in the last fifty years Occasionally a sporadic case having the clinical characteristics of a mild typhus fever would be recognized in our clinics, and following Brill's[1] description of a mild endemic typhus like disease in New York City, we in Baltimore grew accustomed to call such cases instances of Brill's disease, though we reported them to the Health Department as typhus fever Brill drew attention to the fact that these cases were sporadic, affecting only one person in a family, that they occurred usually in the summer season, that the exanthem was rarely hemorrhagic, and that the mortality was not more than 2 per cent Inclined at first to differentiate this condition from both typhus and typhoid as a new disease, he was ultimately led, through the immunological evidence adduced by Anderson and Goldberger[3] and others, to accept its close relationship, if not its identity, with typhus Brill suspected, however, that some vector other than the body louse was responsible for the transmission of this disease Maxcy[4] in 1926 described cases of endemic typhus, or Brill's disease, in the cities of the Southeastern United States and presented epidemiological evidence pointing toward a rodent reservoir of the disease and an ecto parasite of the rat as the probable vector

Brill's and Maxcy's descriptions of endemic typhus fever seemed for some years to satisfy our diagnostic needs in connection with the occasional sporadic case seen in Baltimore However, about four years ago it was recognized that a type of typhus-like fever was being seen which, in its place of origin, its course, its apparent mode of transmission, its exanthem, and its mortality rate, differed markedly from the endemic typhus as described by Brill and by Maxcy The case reported below is fairly typical of this group It is one of a series of eight which have been observed by one of us

## CASE HISTORY

Mrs R B , a housewife of fifty-five years, resident in the county near Laurel, Maryland, was sent to the University Hospital on June 14, 1931, by her physician, Dr B P Warren The patient was drowsy and slightly irrational, the following history was obtained from her husband

She was one of ten children, five of whom had died of tuberculosis before the age of thirty The patient, however, had not lived in contact with these tuberculous siblings Her own health in childhood and adult life had been excellent She had borne four living children, two of whom had died of childhood diseases and one as the result of an accident She had had one stillbirth In recent years she had had frequent mild "colds" and a slight chronic cough Slight deafness had been noticeable There had been a few attacks of abdominal pain in the last year which had led her physician to suspect disease of the gallbladder At times there had been some frequency and burning of urination

Seven days before admission she awoke in the morning with dull aching pains in the lower extremities which, together with a feeling of nausea, kept her in bed all day That evening she had a severe chill and about one hour later she vomited Since that time she had been severely ill with fever, accompanied by nausea and the vomiting of all food An eruption appeared over the body on the third day of the disease, which at first was thought to be a drug rash Her physician, however, soon suspected the nature of her illness, since other cases had occurred in his prac-

tice After consultation with the State Health officials she was transferred to the hospital

Her husband stated that the home was free from lice and fleas On either May 30th or 31st, eight or nine days before the onset of symptoms, his wife had told him of having found attached to her neck a brownish tick which she had removed and killed

**Physical Examination**—The patient was a middle aged woman of medium frame, moderately overweight She appeared dull and drowsy, and answered questions irrationally Her face was quite flushed and the conjunctivae somewhat injected The skin was hot and dry A speckled eruption covered the trunk, front and back, the arms and hands, and more sparsely the region of the knees, lower legs, and dorsal and plantar surfaces of the feet The face and neck were spared, there were very few lesions on the thighs This eruption consisted of a base of subcuticular pinkish flushing of lacelike and sometimes linear character At innumerable points on this basic flush were pinhead sized, darker pink spots which on pressure faded almost, but not quite completely Some of these spots were very slightly elevated or papular and a very few vesicular Over the back of the shoulders and the buttocks some of these spots were bright red and frankly petechial A few petechial spots were also seen on the roof of the mouth

The tongue was coated with a white fur The papillae at its tip were brightly injected The lymph glands in the superficial groups were not enlarged The examination of the lungs was negative except for the presence of a few fine râles at both bases, posteriorly The contour of the heart by percussion was normal and the sounds were found clear and regular Pulse 116 Blood pressure 126 mm. Hg systolic and 66 diastolic. The abdomen was slightly distended The spleen and liver were not palpable

Twitching movements of the extremities occurred intermittently These were especially prominent in the fingers and forearms The general muscular tone seemed relaxed There was no cervical rigidity and no Kernig sign. The deep reflexes at the knees, ankles, and elbows were active The pupils reacted

to light There was no Babinski sign The superficial abdominal reflexes were not obtained

**Laboratory Examinations** — *Urine* —Repeated routine tests were negative except for a trace of albumin

June 14th Blood Red blood cells 4,600,000 White blood cells 16,000 Hemoglobin 80 per cent Kolmer test negative Stool examination negative

June 15th Widal test Negative for Bacillus typhosus and paratyphosus A and B

June 15th Blood culture Negative

June 18th Stool culture Negative

June 16th Weil Felix—agglutination positive for B proteus $x_{19}$, in dilutions up to 1 – 100 in one laboratory and 1 – 320 in another

June 23rd Weil Felix—agglutination positive in dilution 1 – 400 in the first laboratory

**Course in the Hospital** —The patient lived for ten days after admission to the hospital The course of the fever is shown in Fig 198 On the tenth day of the disease there was a pseudocrisis with apparent improvement, but after the return of the fever the course was steadily downward Such complaints as the patient made in the first few days were of headache, chilliness, nausea, and pains in the back and legs She was constantly dull and toxic, and for the last few days deeply comatose Twitching, restlessness, and moaning were continuous Some hypertonicity of the arm muscles developed late, but no cervical rigidity and no Kernig's sign appeared There was urinary retention with overflow incontinence For several days the respiratory rate was very slow, 12 to 16, and somewhat irregular This could not be attributed to drugs Frequent vomiting of small amounts continued throughout A distressing hiccough was present There was progressive abdominal distention Constipation was obstinate, but results were obtained with purgatives and enemata In the last three days signs of bronchopneumonia were observed at both bases with a rising respiratory rate, cyanosis, and hyperpyrexia The rash showed no marked extension except

for the appearance of a few spots on the neck and cheeks It changed, however in color and in character The pinkish flush became more purplish over the dependent portions and more

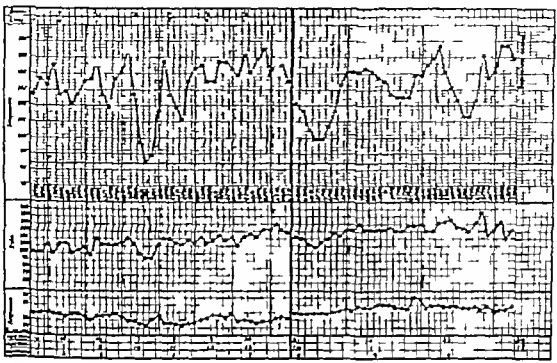

Fig 198 —Temperature chart. Mrs. R. B

blotchy The petechial character of the spots became more evident and the color of these spots on pressure was a dull brown

NECROPSY

Mrs R B , white, female, aged fifty five years Autopsy performed by Dr C G Warner, June 24 1931

Clinical Diagnosis —Tick bite fever

The body was that of a middle aged female, fairly well developed, and moderately nourished There was no evidence of recent loss of weight A diffuse, fading macular type of eruption was present over the torso upper thighs, and neck There were also some petechial hemorrhages in the skin of the neck and of the left arm The eyes, ears, and throat showed nothing unusual There was no general glandular enlargement and no bony deformities were present

The usual autopsy incision was made through the normal amount of subcutaneous fat The peritoneal cavity was found to contain about 100 cc of serous fluid which was colorless and

free from coagulum There was no evidence of any peritonitis The coils of the small intestines were moderately distended with gas

The urinary bladder was markedly distended, its fundus being almost to the umbilicus The spleen extended to, but not below, the costal margin The remaining abdominal viscera were normally disposed and showed nothing on first examination

The thoracic cavity was opened and presented no free fluid in either pleural cavity In the right apical region there were a few rather dense fibrous adhesions which were separated with difficulty

The pericardial sac was opened and showed several petechial extravasations of blood in both the parietal and visceral layers of the pericardium The heart, on removal, was found to weigh 325 Gm , it felt rather soft and flabby in consistency There was no inflammatory exudate on the endocardium or on any of the valves The measurements of the valves were within normal limits The left ventricular wall measured 14 mm in thickness and presented a pale, swollen, washed-out appearance

**Lungs** —The right lung showed a depressed, scarred area on the posterior portion of the apex which contained multiple shotty nodules The basilar portion of this lung presented multiple indurated areas On cross section of the lung, the shotty nodules in the apex appeared to be areas of fibrocaseous tuberculosis The more dependent portion of the lung was confluently consolidated, and in this region the bronchi were filled with a purulent exudate

*Left Lung* —The left lung showed an air-containing apex, the lower lobe presenting a condition similar to that seen in the dependent portion of the right lung, *i e* , a confluent bronchopneumonia

**Aorta** —Just above the aortic valve in the sinuses of Valsalva, arteriosclerotic changes were present in the form of atheromatous plaques under the intima Longitudinal fatty deposits were also found farther down in this vessel

**Liver** —The liver weighed 1650 Gm and on its external surface presented numerous pale yellowish, streaked areas just

beneath the capsule The cut surface when washed free of blood appeared to be pale and swollen

Spleen —The spleen was moderately enlarged, weighing 225 Gm The normal contour and shape were preserved It felt rather soft in consistency and its capsule wrinkled when the organ was placed on the table The cut surface showed a soft semifluid pulp which protruded above the peripheral margin

Gastro-intestinal Tract.—Gross examination of the gastrointestinal tract showed no lymphoid hyperplasia and no ulcerations in the ileum or colon The pancreas showed nothing unusual

Adrenals —The adrenals appeared normal, both externally and on the cut surface

Kidneys —The kidneys were of moderate size, weighing 140 and 150 Gm , right and left respectively They appeared rather pale as observed through the capsule No lobulations were seen and there were no hemorrhages on the cortical surface The capsule stripped readily, leaving a pale, swollen, nongranular surface On cross section both organs presented a widened cortex with a rather indefinite appearance to the normal cortical striations The two anatomical elements, the cortex and the medulla, were well defined

The pelvis of the right kidney was dilated to the extent of about 25 cc. The left pelvis also showed moderate hydronephrosis The pelvic mucosa in each case was congested but contained no exudate Both ureters were irregularly dilated throughout their extent The bladder was distended to about 1 liter, its internal surface showed nothing other than congested mucosa

The female generative organs presented evidence of senile changes

Permission to examine the brain and cord could not be obtained

Microscopical Note —The specimens from this autopsy were preserved in formalin and sections were cut in June, 1931, and stained routinely with hematoxylin and eosin At the end of seventeen months (November, 1932) of 10 per cent formalin

fixation, additional blocks were cut from these specimens Rickettsiae were demonstrated in these tissues by the following method of Pinkerton and Maxcy[15]

The tissues were washed in running water for twenty-four hours They were then fixed for thirty hours in Regaud's fluid to which were added 20 cc of 40 per cent formaldehyde to every 100 cc of Regaud's solution Again, the tissues were washed in running water for twenty-four hours and at the end of this time dehydrated in graded alcohol They were then cleared in chloroform, followed by chloroform-paraffin, and embedded in paraffin in the usual way Sections were cut 5 microns in thickness, mounted on slides, and stained eighteen hours in Giemsa's stain The tissues were stained blue The rickettsiae appeared as minute, dark purple, bacilliform and coccoid bodies within the cystoplasm of endothelial cells of the smaller blood vessels and capillaries of the skin, heart muscle, pancreas, and kidney The excessive stain was removed with methyl alcohol until the greenish tint of the red cells changed to a light pink color At this stage the rickettsiae appeared somewhat smaller and were stained a pale blue color

*Lungs* —Sections of the lung showed a rather patchy accumulation of exudate in the alveoli This exudate appeared to be extremely cellular and was also found within the lumen of the bronchi Several areas of confluent consolidation were present, the exudate consisting of cellular infiltration of leukocytes and fibrin

*Heart Muscle* —Section showed a rather spread-out appearance of the myocardial fibers with little or no fibrosis and fragmentation Giemsa's stained sections of the heart muscle showed rickettsia-like bodies within the cytoplasm of the endothelial cells of the subepicardial and interstitial capillaries

*Liver* —Section of the liver presented a moderate amount of fatty change, apparently without regard to cellular location Scattered foci of necrosis were also seen in the midzone of the liver lobules These foci were composed chiefly of liver cells which had become necrotic A few mononuclear cells were present in these areas, but there was no perifocal inflammatory

reaction Granules of blood pigment were seen in the liver cells, the sinusoidal endothelium and in many of the Küpffer cells

*Pancreas* —The pancreas showed beginning autolytic changes with Giemsa's staining The islets appeared normal and the acini showed nothing unusual Intracytoplasmic rickettsiae were present in a few of the endothelial cells of the interacinar capillaries

*Kidneys* —Sections of the kidney showed a thickened capsule The endothelial cells of the subcapsular vessels were swollen and a few were seen to contain intracytoplasmic rickettsiae The tubules appeared to be dilated In the convoluted portion the epithelium was swollen and granular Many of the glomeruli were obliterated and hyalinized

*Skin* —Sections of the skin contained an occasional thrombosed capillary with only a very slight perivascular round-cell infiltration No hemorrhages or necrotic areas were seen in the epithelium or in the tissues of the subcorium Rickettsiae were readily demonstrated within the cytoplasm of the swollen endothelial cells of the capillaries

**Anatomical Diagnosis** —Rickettsial disease (tick bite fever), fading macular eruption trunk and extremities, subserous petechiae, pleura and epicardium, acute splenic tumor moderate, focal necroses, liver, cloudy swelling of heart, liver, and kidneys, distended bladder, hydro-ureter, hydronephrosis, bilateral, fibrocaseous tuberculosis, right apex, confluent bronchopneumonia lower lobes, bilateral

## DISCUSSION

The clinical aspects of this case correspond very well with those we have observed in 7 other patients and with the cases of similar nature that have been described by Shipley[5] and by Rumreich, Dyer and Badger[6] The onset of the disease is usually abrupt with few or no prodromal symptoms Chills are frequently observed in the first days of the illness The fever rises abruptly and after the first day or so is maintained at a height usually between 103 to 105 F Between the tenth and

the fourteenth day we have several times observed a pseudo crisis, such as occurred in the case here reported In the more fulminating cases, death may occur within the first week but is usually delayed to between the second and third weeks In the patients that recover, the fever usually terminates by gradual lysis, but occasionally crisis is observed Hyperpyrexia is not infrequent

The eruption is commonly first observed between the third and seventh days The true eruption is preceded by a subcuticular, irregular or lacelike flushing The face is more uniformly flushed and has a rather swollen appearance The conjunctivae are injected Over the arms, and later over the trunk, there appear macular and slightly papular spots not very clearly defined and at first fading almost completely on pressure As these grow more pronounced, close observation will frequently disclose a few threadlike, dilated vessels over the center of the macule These constitute the earliest hemorrhagic phase of the eruption Petechial hemorrhage then occurs, obscuring these vessels, and passes through color changes from bright red to purplish and then to rusty brown The rash covers the whole body, exclusive of the face, in most cases (Fig 199) Not uncommonly, lesions are seen on the palms of the hands and soles of the feet Once established, the same lesions persist throughout the course of the disease, but are more pronounced when the fever is highest The hemorrhagic character of the rash is usually first developed over the areas of the body subjected to pressure The eruption is closest set and most nearly confluent over the forearms and wrists In very severe cases, localized areas of skin gangrene may develop over bony prominences In convalescence the rash fades rapidly, it is not infrequently followed by fine desquamation

An essential characteristic of the disease is the multiplicity of nervous symptoms Early stupor and restless delirium are common Tremors and twitching of the face muscles and especially of the forearms and hands may develop within the first week, even in the absence of excessively high fever Headache is frequently present and may be very severe, but on the whole

it does not seem to be as prominent a feature as in epidemic typhus Pain in the back of the neck and in the lower back and legs may be very acute especially at the onset of the disease Meningismus may be very pronounced and may be accompanied by photophobia and generalized hyperesthesia The spinal fluid is usually normal, but may show a lymphocytic pleocytosis

The pulse is usually accelerated in proportion to the fever The pulse, blood pressure, and heart sounds show no charac-

Fig 199 —Case of tick bite fever University Hospital Baltimore August 5–26 1932 Recovered. Note character of eruption on forearms and trunk, eighteenth day of the disease

teristic changes other than those observed in any severe infection

Obstinate constipation seems to be a rather characteristic finding and may, as in the case reported, be accompanied by abdominal distention and vomiting Jaundice has not been observed The spleen is occasionally palpable

At the height of the disease, retention of urine with incontinence is very frequent A slight albuminuria is the rule

A moderate polymorphonuclear leukocytosis is present in the majority of cases The Weil-Felix reaction is usually positive toward the end of the first week, and agglutinations in progressively higher titer are observed as the stage of convalescence is reached

The 8 cases of this type that we have observed showed the following striking differences from the milder endemic typhus of the South Atlantic seaboard All 8 of these cases were either country dwellers (6), or had visited in the country within two weeks before the onset of their illness (2) Endemic typhus, contrary to this, is an urban infection and is largely confined to those living in unsanitary urban dwellings

All of these cases occurred between May and October, *i e*, in the Maryland tick season In 5 of the 8, a definite history of tick bite, within two weeks before the illness, was obtained Two patients were bitten on the neck, one on the back, one on the breast and one had multiple bites In no instance was evidence of lousiness obtained Unfortunately, inquiries as to flea bites were not uniformly made Louse transmission is probably rare in our local form of endemic typhus, the rat flea being more commonly implicated Transmission of the virus of true typhus by tick bite has not been proved

In 5 of these 8 cases, the exanthem was definitely purpuric in character It was usually pronounced about the wrists and forearms, and several times lesions were seen on the palms and soles In these respects the exanthem varied from the rash of endemic typhus which is most pronounced over the trunk and is rarely purpuric

In only one of these 8 cases was a definite crisis observed In 3 others, that recovered, the fever ended by a slow lysis In one case with recovery the late course of the fever is not known In 2 cases the fever persisted for over three weeks and was not entirely normal at the time of discharge from the hospital at the twenty-third and twenty-ninth day Crisis, on the other hand, is a common ending of the fever of endemic typhus, and it is rare for the fever in this disease to persist after the sixteenth day

There were 3 deaths among our 8 cases ($37\frac{1}{2}$ per cent), and in 2 other cases the illness was of a very severe type In endemic typhus the mortality is very low probably less than 2 per cent

It was natural when the association of this disease with country residence and with tick bite became apparent that its possible identity with Rocky Mountain spotted fever should be considered Our observations, as well as those of other clinicians in this and neighboring states were called to the attention of the State Health Department and of the United States Public Health Service, through their efforts evidence has been obtained which has finally proved the existence of an Eastern type of Rocky Mountain spotted fever

It may be of interest to summarize briefly the results of these investigations and to point out the still-existing gaps in our knowledge concerning this newly discovered form of the disease

The clinical similarity of the disease in man in the Eastern states to Rocky Mountain spotted fever of moderately severe grade, has been alluded to by Rumreich, Dyer, and Badger, and also by Shipley The clinical similarity, however, is not strong evidence in favor of the true identity of the two diseases, since even experienced observers state that, on clinical grounds alone a differentiation between Rocky Mountain spotted fever and severe forms of typhus would not be possible The etiologic relationship of tick bite to the Eastern form of the disease may he assumed as proved Forty-eight per cent of the cases investigated by Rumreich, Dyer, and Badger gave a definite history of tick bite. An additional 6 per cent bad crushed engorged ticks removed from dogs, and the remaining cases had all occurred under conditions in which tick bite was possible Of Shipley's 6 cases, 2 gave a history of tick bite In our series of 8 cases a definite history was obtained in 5 Moreover, the study of the seasonal occurrence of the disease in Maryland has shown that it corresponds well with the tick season in this state The cases investigated by Riley and Halliday,[7] and those by Dyer, Badger, and Rumreich,[8] occurred in heavily tick infested localities Moreover, there is a marked tendency for the disease to recur in the same foci in succeeding years No other probable

vectors of the disease have been discovered in relation to the investigated cases

In the Western form of the disease, ticks infected with the virus have been discovered in nature Investigations of the occurrence of the virus in the ticks in the Eastern states have recently been published,[16] and the existence of such a tick virus is no longer a matter of assumption The Western tick (*Dermacentor andersoni*) does not occur in the area of distribution of the disease in the East On the other hand, the common tick of the Eastern states (*Dermacentor variabilis*) has been shown both by Maver,[9] and more recently and conclusively by Dyer, Badger, and Rumreich, to be able to transmit the virus both of the Western form of the fever, and of the more recently discovered Eastern form Since this is the tick most commonly concerned in tick bites in the Eastern portion of the country, there is strong presumptive evidence that it is the actual vector of this form of the disease

In the Western region, the virus of Rocky Mountain spotted fever has been shown by Ricketts,[10] and later by Wolbach,[11] to be transmissible through the egg, larval, nymphal, and adult stages of the wood tick (*D andersoni*) Inasmuch as the adult tick hibernates during the winter and resumes its egg-laying activities in the following spring, the virus may remain active for several seasons in the infected arthropod and its offspring Moreover, it has been shown that in unfed nymphal ticks, the virus is in a dormant or avirulent stage After the nymphs, or the adults which have hatched from these nymphs, are allowed to feed on guinea-pigs, the virus rapidly becomes virulent again or "reactivated" as Spencer[17] says This important observation has led to the development of a tick virus vaccine, which is obtained by grinding to an emulsion either the bodies of infected adult ticks or the bodies of engorged nymphs infected in the laboratory This vaccine is already in widespread use in the Western mountain country, but as yet there are no reports of its administration in connection with the Eastern form of Rocky Mountain spotted fever, nor are there any similar investigations published concerning the immunity-producing qualities of the

virus of the Eastern form of the disease However it has been shown that the infected dog tick (*Dermacentor variabilis*) can transmit the virus to a second generation of ticks

In Rocky Mountain Spotted fever the blood of patients in the active stage of the disease contains the virus which can be transmitted experimentally to guinea pigs Guinea pigs can likewise be infected with the tick virus of the Western form of the disease The guinea pig infected in either manner develops a febrile disease, with characteristic clinical and pathologic manifestations In addition, guinea pigs which have recovered from this infection with the Western form of the virus show immunity to a second inoculation with the same virus They remain susceptible, however, to inoculations with the virus of other types of typhus-like diseases Thus, for example, they are susceptible to the virus of Mexican typhus (Tabardillo), to the virus of endemic typhus of the Eastern and Southern states and to the virus of European epidemic typhus The pathologic lesions produced by Rocky Mountain spotted fever in the guinea pig, and especially the specific immunity produced in this laboratory animal are at the present time the most reliable methods of differentiating the virus of Rocky Mountain spotted fever from that of other diseases of the typhus-spotted fever group

Similar experiments have been carried out by Badger, Dyer and Rumreich,[12] with the virus in the blood of patients who were considered to be suffering with the Eastern form of Rocky Mountain spotted fever It was found that guinea pigs developed a febrile illness with lesions similar to those seen in the guinea pigs infected with the Western virus It was also demonstrated that guinea pigs which had recovered from the infections with the Eastern virus showed definite immunity to subsequent inoculations of the Western virus On the other hand, they were not immune to the virus of endemic typhus, or to that of a strain of European typhus These experiments if confirmed, are strong evidence of a close relationship, if not actual identity, of the virus of the Eastern form of spotted fever with that of the Western form

The human pathology of Rocky Mountain spotted fever is scarcely pathognomonic However, a close similarity evidently exists between the lesions in both the Eastern and Western forms of the disease In the Western form, intracellular bodies in the blood were first described by Ricketts [13] These bodies, later named *rickettsiae* in his honor, have been studied more intensively by Wolbach, who suggested the name *Dermacentrovenus rickettsi* for these micro-organisms and conclusively demonstrated their etiologic relationship to Rocky Mountain spotted fever He

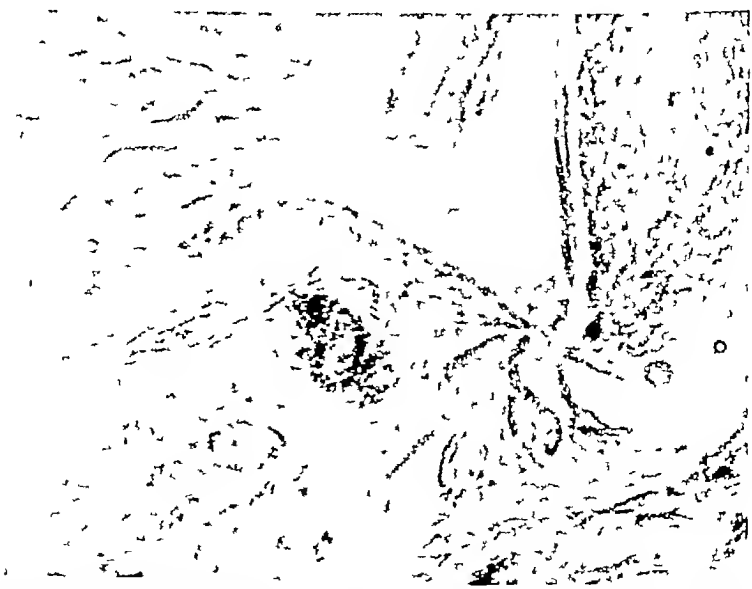

Fig 200 —*Rickettsiae* bodies Section of skin, Giemsa's stain Note intra cytoplasmic rickettsiae Magnification × 1050 Mrs R B

differentiated this organism from other forms of rickettsiae, notably the *Rickettsiae prowazeki* of European typhus Wolbach and others have shown the presence of *Dermacentrovenus rickettsi*, not only in the human, but also in the infected ticks and in the lesions of experimental animals infected with the Western strain of the virus

In respect to the rickettsial nature of the Eastern form of the disease, little published evidence has so far been offered About a year ago, Lillie[14] reported the autopsy findings of 5 cases but

made no special search for rickettsiae, although he did find in several instances clumps of minute, basophilic rod shaped inclusions in swollen endothelial cells of thrombosed capillaries in the skin, thyroid, liver, and brain More recently, Harris[18] demonstrated *rickettsiae* in the human skin, in a case occurring in Tennessee. These rickettsia like bodies, however, have not been mentioned as having been identified in the tissues of the guinea pigs, nor of the ticks experimentally infected with the Eastern form of the disease In the three autopsies which have been performed in our series of cases, the tissues have been studied by special methods, and in each instance what appear to be definite rickettsiae have been found (Fig 200) In addition, we have demonstrated rickettsiae in a skin biopsy from another case of the disease in Maryland

In summary, then, it seems that in clinical form in nature of the vector, in behavior of the virus in the guinea pig and in the type of immunity produced, the typhus-like disease observed in the Eastern states in recent years has been shown to be closely affiliated with Rocky Mountain spotted fever In view of the relatively high mortality of this disease in the East and of the apparently increasing number of cases reported each year it is evident that the spread of this virus in the heavily tick infested regions of the Eastern coast may come, in the future, to present a public health problem of considerable magnitude

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## CONTRIBUTION BY DR CHARLES R AUSTRIAN

BALTIMORE

### BRONCHIECTASIS[1]

OF the two topics, bronchiectasis and neoplasms of the lung, suggested to me by your secretary, I have chosen the former primarily because it is a condition that occurs more frequently than it is recognized, and secondly, in order to indicate that if a timely diagnosis of it is made, beneficial therapy can be instituted It was Lincoln Steffens, I think, who remarked that to teach any subject demands less the imparting of what is already established as knowledge and more the arousing of interest to inquire of what is unknown or in doubt The truth of this remark cannot be gainsaid but if Laennec's statements set out in his original description of bronchiectasis had been appreciated and transmitted to each generation of physicians since his time, much that passes as new would be relegated to its place among established facts and investigation could be directed to unclarified aspects of the subject.

Read if you will Laennec's accounts of the cases observed by him and by Cayol, or review the writings of Barth and of Trousseau. You will marvel to find in them observations concerning morbidity, symptomatology, differential diagnosis, and variability of signs, many of which have been rediscovered in recent years

It is conservative of assert that ordinarily when reference to bronchiectasis is made, one pictures a state in which there is a history of chronic cough productive of large quantities of purulent sputum, of recurrent hemoptysis of variable size, of periodic

[1] Clinical Lecture before the Williamsburg Medical Society Brooklyn N Y November 14 1932

febrile attacks diagnosed as bronchopneumonia, and in
examination discloses pallor, good nutrition, and signs
tensive infiltration or excavation and fibrosis of the lungs

It is to be emphasized that these evidences are those
advanced stage of the disease, to prevent the developme
which should be the endeavor of the profession, a result
achieved only if it learns to recognize the state in an e
phase of its evolution

A diagnosis of bronchiectasis should be considered, tenta
at least, in all cases of chronic or of recurrently productive
that occurs in individuals who maintain good nutritio
bodily vigor in spite of those symptoms The output of sp
need not be large nor the physical signs of bronchopulm
disease many, to warrant that working hypothesis

At first, cough may be seasonal only It may occur in p
of short duration, to recur at intervals more or less brief
itially, it may be nonproductive Later it may lead to th
pulsion of small amounts of material, and later still to th
pectoration of as much as 20 or more ounces of sputum i
course of a day But, early or late, the amount of sputum i
daily even if it be not large is likely to be influenced by ch
of position The material coughed out is purulent It m
may not contain elastic tissue but unless there is an assoc
tuberculosis, it will not contain Koch's bacillus It has a si
ing, sweetish odor but it is not usually foul In excep
cases there may be marked fetor of the sputum and of the br

Hemoptysis, single or multiple, is a cardinal symptom
occurs more frequently in this disease of the lungs than in
other with the possible exception of phthisis The bleeding
be scanty or profuse but it is rarely of sufficient magnitu
of such frequency as to cause a marked anemia A dry, he
rhagic type of bronchiectasis has been described by Benza
and Azoulay in which cough and expectoration seldom occu
recurrent bleeding from the bronchi is the only symptom
develops

Unlike pulmonary tuberculosis, bronchiectasis is accomp
by but few constitutional symptoms except when the disea

extensive or of long duration, a diagnostic fact of importance Fever is inconstant or slight except during recurrent attacks with evidences of localized consolidation or in those instances in which there are marked globular dilatations of the bronchi, that give rise to the same anatomical conditions as cavities Then it may be high and either remittent or intermittent A slight leukocytosis is the rule Clubbing of the digits is met with regularly Acropachie or general osteoarthropathy develop only in cases of long duration and in those with marked saccular dilatation of the affected bronchi In both of these groups, extreme hypertrophic changes in the extremities may be encountered Although sinusitis and oral sepsis are regular concomitants, laryngitis does not develop frequently

The thoracic signs are extremely variable. In those advanced cases in which the pathologic changes are widespread and in which saccular widenings of the bronchi are large, the evidences of pulmonary excavation will be demonstrable. If there is extensive scarring and infiltration of the interbronchial parenchyma, there will be signs of fibrosis and patches of consolidation that are most frequently basal To enumerate in detail the evidences of these changes is unnecessary here, but it does seem well to point out and to emphasize the fact that in many cases of bronchiectasis and in most of those in which a diagnosis made may mean a favorable therapeutic outcome, these local manifestations may be lacking almost *in toto* Individual cases are frequent in which the physical examination is negative because the pathologic process affects only bronchi that are deeply situated Others are met with in which a complicating or associated disease such as tuberculosis or bronchitis masks the bronchiectasis Particularly if there is a marked grade of emphysema, even extensive ectasia of the bronchi may escape detection unless the presence of clubbing of the digits leads to the thought of its presence

Of real aid early to establish the existence of what may be a remediable bronchiectasis is the recognition of the fact that the disease should be considered when, in association with the symptoms referred to already, physical examination of the chest

discloses no abnormality at all or only a trifling diminution of resonance with persistent or recurrent moist râles The adventitious sounds may escape detection unless auscultation is practiced before and after the patient's position is changed The paucity of the signs, limited as a rule to the inferior part of the lungs, with the abundant symptoms, is indeed most suggestive and is the ground for further study Such investigation will lessen the unwarranted frequency of the conclusion that a given clinical picture is due to a so-called "chronic bronchitis" or to tuberculosis It is to be remembered that in the early stages, the pathologic changes are limited frequently to one lung or even to one lobe of a lung and that transmission of adventitious sounds to the opposite side may lead to the erroneous conclusion that the process is a bilateral one When the changes are unilateral, it has been our experience that they are localized most frequently in the lower lobe of the left lung This is due perhaps to the evolution of the malady of a chronic nontuberculous infection there, perhaps because the angle of origin of the left inferior bronchus is a more acute one than that of the right or because it is crossed by the pulmonary artery and impinged upon by the heart

The course of the disease is a chronic one but generally it is only mildly debilitating However, despite the little systemic disturbance it causes, bronchiectasis leads so often to all but complete ostracism that the consequences of it are most distressing If the issue is a fatal one, death may be the result of pulmonary suppuration, of bronchopneumonia, empyema, abscess of the brain, sepsis, emyloid disease or of circulatory failure The mortality is highest in childhood and many of the affected children die before the age of puberty

The morbidity of bronchiectasis has certainly been underestimated So long as the diagnosis of it was based solely on clinical and anatomical grounds it was regarded as a relatively uncommon disease, first because the physical signs are misleading in many cases, secondly, because the lesser grades of bronchial dilatation are readily overlooked and even appreciable changes escape detection unless the bronchi are explored to

their ends when a postmortem examination is made thirdly, because simple roentgenography fails in many cases to reveal the presence of the condition It is so usual for a plain film to disclose no abnormality, that in equivocal cases this negative finding is presumptive evidence of the presence of bronchiectasis

The failure of unaided roentgenography to show even very considerable abnormalities of the bronchi may be due to one or more of several causes If there is only slight thickening or infiltration of the bronchial and peribronchial tissues or if there is only a small amount of exudate within the affected tubes when the examination is made, a plain film may fail to picture any significant shadows So, too, the essential changes within the bronchial tree may be obscured by the shadow of the heart, of the diaphragm or by that of some other pathologic state

The inadequacy of ordinary roentgenography was lessened when it became practicable clinically to demonstrate the ramifications of the tracheobronchial tree This was accomplished by x ray photography of the thorax after an opaque substance was caused to enter the lower air tract Several different materials have been utilized for the purpose and of these, iodized poppy-seed oil or lipiodol is the one that has been adopted generally Although this foreign substance can be demonstrated in the bronchi for more than ten months after its instillation, apparently no harmful changes are caused by it and some observers have even attributed a therapeutic value to it

The oil may be introduced into the bronchi according to any one of seven different methods The information afforded by the bronchographs will depend less on the special method employed than it will upon the observance of certain details Among the latter, one in particular is cardinal. If a localized change is to be visualized it is important that the portion of the chest in which it is situated should be dependent when the oil is introduced, for experiments to show the distribution of particulate matter made to enter the lower air passages have demonstrated the influence of gravity upon the deposition of such foreign material

So far as I know, the variations of the normal bronchial

arborizations have not yet been established by this procedure Such observations are needed before slight but perhaps significant changes can be detected and interpreted properly

Bronchography has made it possible to demonstrate slight dilatation of the bronchi, to determine the distribution and extent of the change and to identify several types of bronchiectasis Three main varieties of the disease have been described (1) Uniform or cylindrical dilatations of the bronchi in which the divisions of the air tubes, instead of showing a gradual lessening of diameter, maintain a uniform width throughout their length This type is usually bilateral and involves the bronchi to the lower lobes especially (2) A fusiform type in which these widened branches have terminal bulbous enlargements (3) A saccular variety in which the branches are dilated sufficiently to give rise to the appearance of single or multiple cavities of varying size or in which beaded shadows result from irregularly distributed widenings of a bronchus at intervals along its spread This variety involves often one lung only or even but one lobe of a lung The individual saccular dilatations vary much in size and the pulmonary tissue about them shows considerable infiltration or fibrosis If this type of bronchiectasis is limited to the upper lobe of a lung, it may be indistinguishable from a tuberculous vomica Of these three sorts of dilatation, the cylindrical and the saccular occur most frequently

By means of bronchography it has been demonstrated that in its early stages at least bronchiectasis is limited to one side in from 50 to 70 per cent of the cases studied The frequency with which the unilaterality of the process is demonstrable by this method, as contrasted with the incidence disclosed by physical examination, is referable, as stated, to the confusion engendered by the transmission of adventitious sounds from the diseased to the normal hemithorax

The method of contrast roentgenography should make it possible to diagnose bronchiectasis at a relatively early stage of its development and to localize the site of the pathologic process If these data are acquired, it is to be hoped that treatment may be more efficacious

In several instances, the demonstration in a plain film of a triangular shadow at the base of a lung with its median margin in the posterior mediastinum and its lower one on the diaphragm proved, after the introduction of lipiodol, to be due to a mass of dilated bronchi in an area of collapsed lung A similar appearance has been described by Sparks and was interpreted by him as the evidence of atelectatic bronchiectasis

Bronchoscopical exploration is of value in the study of advanced cases of the disease, especially to determine whether or not a local atresia, scarring, membrane formation tumor or foreign body is the cause of a secondary dilatation distal from the obstruction or to institute therapeutic drainage of secretion As a means of investigating the less extensive, more peripheral involvement of the smaller tubes, its utility is limited except in so far as it may show into what larger branches the secretion is flowing Characteristically, in this disease the bronchi appear wider than normal, the mucosa is turgid swollen and obscured in many cases by adherent, purulent secretion

**Etiology and Pathogenesis**—The relative importance of several factors in the production of secondary bronchial dilatation is moot except in those cases in which clearly identifiable causes are found Important among these are narrowing of the bronchi, congenital or acquired, constriction due to endo- or to peribronchial pressure, obstruction within the lumen of the tubes, to lack of support of the bronchial walls or to traction upon them There is a distinct type of congenital bronchiectasis to explain the occurrence of which many hypotheses have been advanced such as congenital malformation or congenital weakness of the bronchial walls, congenital cystic disease of the lungs, a collection of fluid within or a fetal adenoma of the bronchioles, intrauterine syphilis, etc.

The etiology and pathogenesis of the primary condition requre further study Experience has led me to think that though doubtless heredity is an etiologic factor in this group in the same sense that "constitution" or "diathesis" is in many pathologic states, it is of relatively less importance than is infection that leads to destruction of the essential elements of the bronchial

walls This view was advanced in 1837 by Stokes and championed in 1891 by Fox Some of the facts that indicate the infectious origin of bronchiectasis are the following

1 The frequency with which there is a history of antecedent or of concurrent respiratory infection, colds, pneumonia, influenza, sinusitis, pertussis, measles, postoperative pulmonary disease, etc , emphasized by Opie, by Elliott, by Hedblom and others

2 The course and ultimate clinical picture presented by many instances of chronic, nontuberculous infections of the lower lobes of the lungs

3 The development of bronchial dilatation after the aspiration of a foreign body

Of the cases observed in our clinic, pneumonia or bronchopneumonia, sinusitis, chronic nasal infections, measles, pertussis and occasionally oral sepsis, assume the most important predisposing rôles An antecedent pneumonia or bronchitis is considered by some observers a more frequent precursor of bronchiectasis than the other infectious diseases enumerated However, inasmuch as the occurrence and recurrence of pneumonic episodes are usual in the course of bronchiectasis and because the diagnosis of bronchitis is made incorrectly so many times, the precise pathogenetic significance of these two maladies is not established Within recent years many observers have emphasized the causal rôle of sinusitis, not merely because of the frequent association of bronchiectasis with it but because of the occasional regression of the bronchial symptoms after the infection of the paranasal sinuses has been overcome

The exact manner in which *mechanical* factors lead to dilatation when infection has caused a weakening of the bronchial and bronchiolar walls has given rise to much discussion Theoretically, widening of the tubes will result when the normal difference between intrabronchial and intrapleural pressure is increased, when there is actual traction on the bronchial walls or when these two conditions coexist In health, the intact bronchial walls are called upon to resist the dilating force of atmospheric pressure less the negative intrapleural pressure In any

state in which the positive pressure within the bronchi is raised or in which the negative pleural pressure is increased the dilating force will be correspondingly augmented and the bronchial tubes will be widened unless they have sufficient resistance to overcome this higher tension In atelectasis—congenital or acquired—the negativity of intrapleural pressure is increased The dilating force of the pressure of the air in the bronchi is thus relatively enhanced so that if the walls of these tubes have been weakened by disease or through developmental fault, dilatation is almost certain to result Similarly, as Corrigan pointed out, when there is marked fibrosis and retraction of the lung, traction is exerted on the bronchial walls and the distending force is increased by the dislocation of the mediastinum and diaphragm as it is in atelectasis In addition to these factors there are to be mentioned the influence of retained viscid secretions and the changes of endobronchial pressure during coughing Hedblom has pointed out that the dilating influence of forced expiration when the glottis is closed is relatively unimportant for then the pressure is elevated without as well as within the bronchi He attributes the baneful consequences of tussive effort to the deep inspiration before the act when there is the maximum disparity between endo and exobronchial pressure

It has been suggested by Ochsner and by Hudson that the earliest change caused by infection is simply a loss of tone of the musculature of the bronchi for serial bronchographs made at intervals of one second showed abolition of the normal peristaltic movements of the bronchial tubes As the disease progresses, the several constituents of the walls are destroyed and are ultimately replaced by fibrous tissue. Whether there be atony or deterioration of structure, the distending influence of the mechanisms described would result in changes that differ in degree only

To assume that the development of the state is inevitable when specific microbic invaders attack the bronchi may or may not be justifiable The trend of current opinion, based on such studies as those of Smith, of Hedblom, of Kline and others, to regard anaerobic organisms such as spirilla, spirochetes, fusi-

form bacilli, etc , as the specific bacteriological causes of the disease predicates the assumption that the failure to demonstrate this group of invaders in a percentage of the cases studied is due to faulty technic or to an overgrowth of them by secondary parasites Neither of these premises, however, seems necessary Such experimental observations as those of Rivers and of Wintemitz, for example, showed that the influenza bacillus may cause necrotizing lesions of the bronchi that penetrate the entire thickness of their walls and form fissures extending from the lumen of the bronchi to the alveoli When this change resulted, retained secretions, gravity and tussive effort led readily to dilatation and sacculation that was a true ectasia

It is our impression that no single group of infectious agents can be considered the *specific* cause of bronchiectasis Bacteria such as hemophilus influenzae, various strains of streptococci, staphylococci and pneumococci, as well as the class of spirochetes, spirillae, fusiform bacilli that are part of the buccal flora may lead to the pathologic basis for the development of bronchiectasis Given such a basis, it seems scarcely necessary to have such accessory dilating factors as traction or increased intrabronchial pressure to bring about dilatation of the bronchi and bronchioles

**Differential Diagnosis** —If the history is characteristic and the signs are outspoken, the diagnosis of bronchiectasis is made readily If the anamnesis is only suggestive and the signs are equivocal, contrast roentgenography will reveal the presence of the condition However, the mere demonstration of dilatation and infection of the bronchi and bronchioles does not suffice It is necessary to determine in so far as possible the underlying cause of the condition and to differentiate from bronchiectasis numerous intrathoracic states that may give rise to symptoms and to signs that simulate it Among the latter, the following merit reference

Tuberculosis of the lower lobes without involvement of the infraclavicular or apical regions is usually a progressive disease with marked toxic or constitutional symptoms, deterioration of general health, dyspnea, and cyanosis Oftentimes a history

can be obtained of intimate prolonged exposure to tuberculosis in childhood, of chronic otitis media or adenitis or of keratitis Tubercle bacilli are usually demonstrable in the sputum elastic tissue may be found as well and a lymphocytosis is more usual than a leukocytosis Although clubbing of the digits may develop, it does not as a rule unless there is a cavity or fibrosis with a secondary bronchiectasis The roentgenograph may show the presence of an active or of an old healed focus elsewhere in the lungs or in the mediastinum, and the response to tuberculin may be outspoken A careful consideration of the history, of the physical findings and of the results of the study of the sputum and the blood should minimize the unnecessary frequency with which tuberculous and nontuberculous disease of the lower lobes of the lungs are confused If the bronchiectasis is localized in the upper third of the lung the differentiation from tuberculosis may be extremely difficult but the continued absence of tubercle bacilli from the sputum, the mildness of the somatic symptoms and the roentgenographic findings are the means to differentiate it from phthisis If bronchiectasis has developed as a consequence of fibrosis of the lungs due to tuberculosis collateral evidence of chronic, extensive pulmonary disease or the demonstration of tubercle bacilli in the sputum will indicate the underlying cause of the bronchial dilatation

Chronic bronchitis is secondary as a rule to some other discoverable pathologic state It occurs more often in middle or in old age and in addition to a seasonal cough is characterized by dyspnea of varying severity and an absence of fever, of hemoptyses, and of constitutional deterioration When of long duration it may lead to the development or to the aggravation of emphysema or may be followed by bronchiectasis The pathognomonic physical finding is the presence of bilaterally distributed rhonchi or of moist râles and at times a prolongation of expiration without any diminution of pulmonary resonance If the output of sputum is large, examination with the roentgen ray after the intratracheal introduction of lipiodol shows in uncomplicated cases no infiltration of the parenchyma of the lungs and no more than a slight widening of the bronchial rami

fications Contrast roentgenography utilized more frequently would doubtless lead to a revision of the diagnosis of many cases classified as bronchitis on clinical grounds alone

Mycotic infections of the lungs, although they are of relatively infrequent occurrence, present now and again a real diagnostic problem for not only do they cause infiltration and fibrosis but bronchitis and bronchiectasis as well However, the presence of more or less characteristic dermal lesions in blastomycosis, sporothricosis and coccidiosis and of discharging sinuses about the neck and chest in actinomycosis should suggest an infection with a fungus and lead to a search for it in the accessible lesions as well as in the sputum

Tumors of the bronchi and lungs give rise occasionally to local thoracic signs similar to those of primary bronchiectasis, but the collateral evidence suffices usually to differentiate between them Benign tumors of the lower respiratory tract are met with rarely and when they are present, the roentgenograph and the bronchoscope serve best to identify them Primary malignant neoplasms lead to gradual or at times to rapid impairment of health and of nutrition, to dyspnea, thoracic pain, and to the development of anemia If the new growth occludes a bronchus, there will be the signs of atelectasis or if it invades the pulmonary tissue the signs of infiltration will increase Usually bacteriological, roentgenographical and bronchoscopical studies will indicate the diagnosis in doubtful cases Metastatic tumors of the lungs are to be suspected if atypical pulmonary signs are found, especially when there is a malignant growth of the adrenal glands, the prostate, stomach, breast, thyroid, or testicle The constitutional reaction of the patient, the anemia and the sharply circumscribed, round or oval, usually multiple uniform shadows shown in the roentgenograph are diagnostic Doubt should arise only in those cases in which bronchorrhea occurs

Pulmonary suppuration—abscess—may be very difficult to distinguish from bronchiectasis The history of the development of the symptoms consequent upon a surgical operation, the aspiration of a foreign body, pneumonia or thoracic trauma may indicate the nature of the disease even when the local signs are

inconclusive The onset of this syndrome is generally more abrupt, the constitutional reaction is marked, irregular fever sweats, chills, leukocytosis, and anemia with localized signs of pulmonary infiltration and excavation are decisive criteria

The syndrome that follows the rupture of an empyema into the lung may be identical symptomatically with that of a bronchiectasis The history of a sudden and unexpected expectoration of a large amount of pus, the more severe general reaction the extent of the pleural changes, the deformity of the thorax, and the roentgenographical appearance suffice usually to clarify the problem and to demonstrate the origin of what bronchial changes may have developed

Of especial interest and importance are certain instances of encapsulated interlobar empyema of which the roentgenographical appearances in films made by projection of the $x$ ray in the usual anteroposterior, postero-anterior or lateral positions resemble so clearly those cast by infiltrative pulmonary lesions, inflammatory or neoplastic, or by thickened, widened bronchi that the true nature of the pathologic change may not be suspected To facilitate the identification of such pleural extravasations, the rays should be projected sagittally in the direction of the several interlobar fissures in the so-called "Kreuzhohlstellung" If this method is employed, densities with more or less ill-defined margins that in the ordinary film seem to be within the substance of the lung will appear as oval, circular, or tapering linear shadows, in the position of the pleural septae that subdivide the lungs

The very characteristic multiple, circular or oval shadows in many of which definite fluid levels are seen in roentgenographs of congenital cystic disease of the lungs can be differentiated best from the somewhat similar ones viewed in films of certain rare cases of bronchiectasis, by the history and the physical examination

Chronic nontuberculous basal infections, first described by that name by Fowler in 1898, may have a history and give rise to localized signs in the lower lobe of one or of both lungs identical with those of an early or slight bronchiectasis In these infections as in bronchiectasis a chronic cough is interrupted by periods of

remission, and febrile bronchopneumonic episodes or hemoptyses occur from time to time These symptoms have little influence on the state of general nutrition Clubbing of the digits is usual Furthermore, the paucity of the physical signs and their localization in the lower lobe of the left lung if they are unilateral, are sources of diagnostic difficulty that may be insurmountable even when contrast films are made These data and the occasional evolution of the syndrome into recognizable bronchiectasis make the idea tenable that in some instances the two may be stages of one malady Prompt recognition of the earlier phase with institution of therapy is needed therefore to prevent the development of the advanced stage

If bronchiectasis develops secondarily to pneumonoconiosis, the history of exposure for years to the inhalation of abrasive dusts, the dyspnea, the bilateral extensive distribution of the signs and the uniform mottling and striae seen in the roentgenographs will reveal the underlying cause of the changes Asbestosis of the lungs, a particular form of pneumonoconiosis that has attracted interest of late, occurs in workers in asbestos, leads to cough, hemoptysis, extreme dyspnea and to emaciation that is out of proportion to the signs of pulmonary disease The examination of the sputum may show the presence of characteristic, golden yellow "asbestos bodies" and the roentgenographs show often obliteration of the costophrenic angle and have a ground-glass or finely mottled appearance, the evidence of a fine fibrosis of the lungs

The origin of bronchiectasis that follows upon the occlusion of a bronchus by a foreign body, can be identified by the history of onset, the signs of atelectasis and by the roentgenographical and the bronchoscopical findings Similar evidence in conjunction with hemotological, general clinical and radiographical studies will clarify the problem when the bronchi are obstructed by a mediastinal tumor

**Treatment**—Until recently, attempts to find a curative treatment of bronchiectasis have been desultory due perhaps to the fatalistic attitude engendered when the diagnosis was established and because of the inefficiency of the many procedures

that had been tried The time honored methods were directed primarily toward a relief of symptoms Although inhalations of steam or of volatilized medicaments and the oral administration of derivatives of the creosote or of the sedative groups give comfort to many patients, neither these nor a host of like measures remedy the underlying basic faults Now and again, general roborant measures or a change of residence to rural districts or to places with a dry and equable climate are beneficial

When it is appreciated that the clinical symptoms in bronchiectasis are attributable in the main to infection, it becomes apparent that the attainment of three major aims should be sought (1) Eradication of the infecting agent, (2) adequate drainage of the bronchi until the sterilization has been brought about and (3) correction of the physical conditions that tend further to widen the weakened bronchi and bronchioles

*Removal of Infection*—Local infections of the upper air passages and of the mouth should be sought for and eradicated Particular care should be observed to combat disease of the paranasal sinuses If bronchial obstruction exists it should be corrected bronchoscopically

To that group of patients in whom bacteriological studies of the bronchial secretion have demonstrated a given coccus or bacillus to be the sole or the predominating organism, injections of autogenous vaccines may be given in an attempt actively to immunize the host It is desirable that the material studied be obtained through the bronchoscope and washed thoroughly before it is introduced into culture media This form of treatment although reported now and again to be helpful has been followed by disappointing results

In the group in whom the spirochetes, spirillae, vibrios, and fusiform bacilli constitute the flora in the bronchial secretion, the introduction of an arsphenamine intrabronchially and intravenously has been followed by definite improvement in some and by a cessation of symptoms in a few others As a rule, 0 4 Gm of the drug in 10 cc of distilled water is instilled through a bronchoscope and a like amount is injected into a vein The treatment is repeated at weekly intervals as often as may be needed

*Drainage*—During the period in which vaccine or an arsphenamine is administered, drainage of the bronchi is favored by utilization of Garvin's postural method or by means of bronchoscopical suction The former procedure causes less discomfort to the patient and if he is taught to assume an inverted or semi-inverted Trendelenburg position for fifteen to thirty minutes three or four times daily mechanically to remove the secretion from the bronchi, the repeated utilization of the bronchoscope may be obviated

Such conservative measures may lead to increased comfort If they are utilized at a time when the bronchial changes are slight and before permanent atelectasis or extensive fibrosis has developed, they may suffice to bring about a symptomatic cure However, at present the diagnosis of bronchiectasis is seldom established at this early stage and it is necessary directly to combat the dilating influence of one or both of these two latter forces to stay the progress of the disease The reduced intrapleural pressure caused by permanent atelectasis or pulmonary fibrosis and the traction on the bronchi in cirrhosis of the lung can be lessened if the affected tissue is relaxed or compressed This has been accomplished in a number of ways and it has been demonstrated by means of contrast films that dilated bronchi can be collapsed even in those cases in which scarring of the lung was extensive The surgical procedures that have been utilized include induced pneumothorax, paralysis of the phrenic nerve, extrapleural thoracoplasty, and lobectomy

Artificial pneumothorax offers a means to offset the influence of lowered intrapleural pressure Its use is limited, however, to those cases in which the layers of the pleura are not adherent to one another Favorable results following collapse of the lung by this method have been reported by many authors but because of the need of frequent reinjections of air and of the occasional development of pleural effusions the use of it has been restricted

Paralysis of the diaphragm brought about by abolition of the function of the phrenic nerve whether by section, crushing, exeresis, evulsion or by injecting of the trunk with alcohol, is followed by a rise of the diaphragm and a diminution of the volume

of the thoracic cavity There results a consequent relaxation of the lung with some compression of the basal area The operation is readily done under local anesthesia, entails little risk has no untoward consequences, and in a small series of cases has led promptly to a diminution of cough and of expectoration In several of our cases, improvement has been progressive and followed by symptomatic cure, in others by an appreciable relief of symptoms whereas in some it has been without demonstrable influence Such variability of effect has been reported by Chauffaurd, Rist, Hedblom, Davies, and others Undoubtedly this method is adapted best for the treatment of unilateral early bronchiectasis of the smaller peripheral tubes, but even when there is extensive involvement of deeper bronchi, it may be helpful at times

Of the surgical procedures employed, pneumothorax and paralysis of the phrenic nerve are the simplest but inasmuch as both methods fail to relieve the symptoms or to halt the progress of many cases of bronchiectasis, thoracoplasty or lobectomy has been resorted to by a number of investigators Neither operation for bronchiectasis has been done in the cases we have studied but none the less the merits of each may be discussed briefly

Extrapleural thoracoplasty is adapted well to bring about permanent complete collapse of the affected lung and thus to negative the malign effects of atelectasis and of fibrosis It has been recommended particularly in these cases in which pneumothorax could not be induced because of adhesions or in which pneumothorax or phrenic paralysis has not modified the symptoms or the course of the malady It is said to be of maximum utility in the unilateral, early cylindrical form of the disease, and in that type complicating fibroid tuberculosis It is considered to be least helpful if there are saccular dilatations located posteriorly The operation of choice would seem to be Sauerbruch's posterior paravertebral resection of the upper eleven ribs in order that sufficient collapse may be produced

Resection of the diseased lung is still a hazardous procedure and though it has been advocated for the treatment of advanced cases not relieved by thoracoplasty, the mortality of the opera

tion is still so high that it is to be considered only as a measure of last resort

Guided by personal experience and by the reading of published data, it is suggested that

1 All patients who have a history of chronic cough productive of purulent sputum, well-maintained nutrition and basal râles should have in addition to a general survey especially careful investigation of the upper respiratory tract and oral cavity, bacteriological and darkfield investigation of the bronchial secretion and a thoracic roentgenograph after the introduction of lipiodol into the bronchi In this way, bronchiectasis may be recognized in an early state, the site, type, and extent of the pathologic process can be determined and the etiology indicated

2 At times development of bronchiectasis may be prevented or the progress of slight bronchial dilatations may be stemmed by the eradication of infections of the upper respiratory and oral passages, supplemented by postural or bronchoscopical drainage and the administration of an arsphenamine in those cases in which spirochetes, etc , are the etiologic factors in a bronchial infection

3 The mechanical forces that produce or increase the dilatation of the air tubes can be combated or offset in large measure by the induction of relaxation or collapse of the lung In some early cases, phrenic paralysis may suffice to bring this about If this fails to accomplish the desired result, it may be followed by artificial pneumothorax or by thoracoplasty Extensive unilateral bronchiectasis may be relieved in some cases by the latter procedures At present lobectomy, primary or secondary, is attended by such danger that it must be considered a last resort in cases that seem to have a hopeless outlook If the disease is bilateral and extensive, none of these or of any other known methods can be expected to accomplish much and symptomatic procedures must be relied upon to make the unfortunate existence of the victim as tolerable as possible

Perhaps none of the foregoing facts is new to you, but if my reiteration of them has indicated the need and the way to recognize the early stages of bronchiectasis, it may be that the solution of some of your diagnostic problems will be facilitated

## CLINIC OF DR GEORGE A HARROP

FROM THE DEPARTMENT OF MEDICINE, JOHNS HOPKINS HOSPITAL AND UNIVERSITY

# THE TREATMENT OF SIMPLE OBESITY

I WISH to present to you today 2 patients suffering from an extremely common disorder, although the underlying cause and the metabolic abnormality involved is as yet poorly understood in many cases

The first patient is a male, aged fifty-eight (Unit number 39153), who was first admitted to our Metabolism Ward September 14, 1931, because of extreme obesity His weight was 329½ pounds (149 7 Kg) and height 68¼ inches (176 cm) His calculated ideal weight was 160 pounds, and he was therefore about 169 pounds overweight His father, who died at sixty seven of heart trouble, weighed 190 pounds, and his mother, who died at fifty seven, had had an average weight of 245 pounds His brothers and sisters are not obese He had been a police man for twenty years, but has done no work for the past twelve years on account of obesity and poor vision In 1930 he weighed 340 pounds and ten years ago 240 pounds For the past six months he had been dieting, and as a result had lost 10 pounds There has been defective vision in the right eye for fifteen years, and two years ago the vision in the left eye began to grow dim For years he has had shortness of breath on exertion and swelling of the legs in the evening, the edema disappearing again in the morning There is nocturia once or twice each night and he has had albumin in the urine for twenty years His appetite has always been ravenous For years he has avoided meats and foods which he thought might add to his weight, but has not restricted himself in the use of starches and sweets of which he is

very fond Of late, especially during hot weather, he has been greatly troubled by redness and painful itching of the skin whenever the skin folds come together He has been married thirteen years, but has no children

Physical examination on admission to the hospital revealed an extraordinarily obese man with a huge pendulous abdomen, thick arms and legs, and with a red active weeping dermatitis wherever the skin surfaces rubbed together There were bilateral ocular cataracts, the one on the right being more nearly mature The breath sounds and heart sounds were poorly heard through the thickened thorax Blood pressure 158/100 mm None of the abdominal viscera could be felt The genitalia were of normal development and appearance The blood showed a moderate polycythemia (5 4 million red blood cells) Wassermann negative Blood nonprotein nitrogen 30 mg per 100 cc, and blood sugar (fasting) 95 mg per 100 cc Basal metabolism test +8 An $x$-ray of the skull revealed a normal sella, and the visual fields were normal in size A glucose tolerance curve (100 Gm glucose), showed the following values in the capillary (arterial) blood Fasting 101 mg, thirty minutes 153 mg, one hour 182 mg, two hours 164 mg, three hours 111 mg The urine showed a trace of albumin and an occasional white cell and cast The urinary concentration and dilution tests showed no abnormalities

His treatment is outlined in Table 1 During the first eight days he lost 9 pounds on a diet of 2000 calories, and 18 pounds during the following twenty-one days on a diet of 1000 calories He was then placed on a rigorous reduction régime for the next six weeks, taking a diet containing but 475 calories daily After eight days of treatment in all he left the hospital having lost 66 pounds in seventy-seven days During this period the urine showed only the slightest trace of acetone bodies on three or four occasions His blood pressure dropped to 124/88 Aside from the first few days he had no great hunger or discomfort, and he was much more active than he had been in years The skin lesions healed completely, the dyspnea disappeared, and his sense of well being improved so greatly that he desired

TABLE 1

J G 58 years

| | Weight lbs | Diet |
|---|---|---|
| *1931* | | |
| Sept 17 | 324 | 2000 calorie diet Protein 110 Gm |
| 25 | 315 | 1000 calorie diet Protein 90 Gm |
| Oct 17 | 297 | Commenced restricted diet Carbohydrate 24 protein, 72 fat 10 Gm Calories = 475 |
| Nov 1 | 282 | |
| 15 | 272 | |
| Dec. 4 | 258 | Discharged from hospital—loss of 66 pounds in 80 days. Diet at home Carbohydrate 90 protein 85 fat 35 Calories = 1015 |
| *1932* | | |
| Jan. 23 | 243 | |
| Mar 5 | 238 | |
| May 14 | 224 | |
| Aug 6 | 211 | |
| Nov 12 | 209 | A loss of 115 pounds in 14 months. |

enthusiastically to continue his diet at home The diet given him for this purpose contained carbohydrate, 90 Gm , protein 85 Gm., fat 35 Gm , 1015 calories On this his weight dropped to 209 pounds during the next eleven months, representing a total loss of 120 pounds in fourteen months

This is an example of a patient with simple obesity of unusual extent who responded well to a régime of extreme undernutrition for eleven weeks, and to a very low diet during the following year The weight reduction was entirely free of clinical evidences of acidosis and was associated with return of the blood pressure to normal levels Both systolic and diastolic levels shared in the fall of tension Moreover the slight amount of albuminuria originally present has entirely cleared up During the period on which the diet was reduced to 475 calories there was a negative nitrogen balance, determined from analysis of the urinary nitrogen, to which 10 per cent was added as the estimated loss in feces, which were not analyzed This amounted to 1 to 2.5 Gm daily He never felt particularly weak during this period or lost his sense of well being The bowels were regular and no cathartics were required

The second patient is a young girl of thirteen (Unit number 42011) with a remarkable familial history of obesity The mother,

65 inches tall, weighs 200 pounds, and a sister of the same height as the patient weighs 236 pounds The maternal grandmother is short, but weighs 210 pounds, and the paternal grandmother, 64 inches tall, weighed 250 pounds at her death from apoplexy at fifty-four, while the paternal grandfather, a baker, weighed 260 pounds Three of the father's sisters have weighed over 200 pounds although the youngest by reducing her diet now weighs much less One of the father's brothers, 67 inches tall, weighs 240 pounds

The patient was not considered to be a fat baby, but at the age of six began to gain rapidly This was coincident with the opening of a bake shop by the father The family came to live above the shop and all of them began to gain weight Her appetite is very good, she is fond of bread and sweets and drinks much water In 1930 she weighed 140 pounds and last year (1931), 180 pounds Her menstrual periods began between ten and eleven and have always been regular and normal Recently she has become very dull and sluggish and takes very little exercise She has done very poorly at school where she has reached but the fifth grade

Physical examination on admission revealed a very large girl, with fat generally distributed and without specific localization Large pendulous breasts and nipples, and a thick abdominal pad were present The heart and lungs were clear Blood pressure 138/94 mm The skin was of normal color and texture and the hair of normal quality and distribution The external genitalia were of normal size and appearance, and there were transverse crines The fingers tapered somewhat and were quite short There was no edema

Studies in the hospital, aside from the occurrence of extreme obesity during puberty, give no support to a diagnosis of an endocrine disorder, except that the basal metabolism was −32 per cent An x-ray of the skull showed a normal sella and the visual fields were normal There was no anemia, the nonprotein nitrogen, sugar, and cholesterol of the blood were normal

Her course in the hospital is indicated in Table 2 Admitted on February 29th, weighing 220 pounds (100 Kg), she lost 11

TABLE 2

E. M. 13 years

| 1932 | Weight lbs | Diet |
|---|---|---|
| Feb. 29 | 220 | Carbohydrate 34 Gm. protein 38 Gm. fat 13 Gm. 405 calories |
| Mar. 10 | 209 | Carbohydrate 24 Gm. protein 31 Gm. fat 10 Gm. 310 calories |
| 21 | 202 | Thyroid extract 64 mg. daily commenced |
| 30 | 198 | Thyroid extract 32 mg. daily |
| May 14 | 187 | Thyroid extract 16 mg. daily |
| 20 | 179 | Discharged from hospital—loss of 41 pounds in 90 days. Diet at home: Carbohydrate 80, protein 50, fat 14, calories 526 |
| June 24 | 175 | |
| Oct. 15 | 162 | A loss of 58 pounds in 15 months |

pounds on a 1000 calorie diet which was then reduced to approximately 300 calories (carbohydrate, 24 Gm., protein 31 Gm., fat, 10 Gm.), and on leaving the hospital on May 21st she weighed 179 pounds, a loss of 41 pounds in eighty-one days. On account of the lowered basal metabolism she was placed on thyroid extract (Armour's) three weeks after admission—at first 64 mg. a day. On account of tachycardia this was reduced to 32 mg. and then to 16 mg. which was given until her discharge from hospital. On the very low diet she remained throughout her stay in nitrogen equilibrium with the exception of the first two weeks, when a loss of 2 to 5 Gm. per day was noted. She remained quietly about the ward and refused to take exercise without urging. No discomfort or weakness was complained of and acetone bodies did not appear in the urine. After she returned home she was continued on a low diet (526 calories) and the weight was reduced to 162 pounds on October 15th, five months later. The basal metabolism determination fell within normal limits (−9 per cent). The mother was quite faithful in following directions, and in order to keep the child from temptation, placed the entire family upon a similar diet. As a result she herself lost 30 pounds, and the 236-pound sister, aged sixteen, lost 50 pounds. It is, of course, evident that our patient has not followed her diet directions strictly, but from conversations with the mother it is quite clear that the diet has not exceeded

1000 calories during the past five months Her improvement mentally has been highly satisfactory, although she is still sluggish She goes to school, however, and is an average pupil, maintaining her grades in a satisfactory manner

Obesity is usually classified either as "simple" (exogenous) in origin, or endogenous, a term usually implying an underlying endocrine basis for the disorder "Simple" obesity is considered to be due solely to overeating and underexercise, habits often superimposed on a familial tendency to physical sluggishness and an hereditary liking for good food

In all types of obesity, whatever the underlying basis, it is evident that the immediate cause of the fat accumulation is an ingestion of food in excess of the metabolic utilization, the requirements of the law of the conservation of energy are inexorable It is equally evident, however, that many obese persons are not extraordinarily heavy eaters Many observations have shown that such individuals may not lose weight or lose weight with great difficulty even if their usual food allowance is considerably curtailed This is well illustrated in the case of our second patient who during five months after leaving the hospital lost but 17 pounds, although on a diet quite certainly of less than 1000 calories It is also clear that efforts made so far to demonstrate a typical metabolic abnormality to which the etiology of all or many cases of obesity may be referred have not been convincing There is no diminished "cost of digestion," or specific dynamic action of proteins or fats in obese persons Their metabolism follows the same path as that of leaner persons All that can be said is that most of them appear to live more economically of energy than do their thin associates It is a paradox in this regard that every motion must entail a greater expenditure of energy in the fat person than it does in the thin individual

The question of an endocrine element in the obesity of the young girl is not definitely settled The occurrence of obesity symmetrical in distribution, appearing very early and with some evidence of precocious sexual development as indicated by the early menses possibly suggests suprarenal involvement more

than that of any other gland There is however a familial tendency to early menstruation The satisfactory response to dietary measures and lack of other abnormalities give slight substantial support for this view Thyroid extract was used because of the low basal metabolism, but was not continued because tachycardia appeared without much result on the weight We hesitate in any event to use thyroid extract in such a young subject, although it may be indicated later It is common experience that obesity of endocrine origin is far more frequently suspected than demonstrated, and the satisfactory response to dietary treatment, as was obtained in this girl, often results in dispelling the suspicion

It is a fact that obesity tends to occur in certain periods of life associated with changes in sex activity which suggest an endocrine basis Such is the overweight which often occurs in young girls during adolescence and usually disappears before twenty The rapid increase in weight after childbirth is well known, as well as the increase which occurs during middle age especially after the menopause, and which is so commonly observed as to be considered a normal event

The endocrine glands which have been implicated in the causation of obesity are the gonads, the thyroid, the pituitary, and the adrenal Certain endocrine maladies affecting these glands are well defined and can be diagnosed with assurance, but their number is limited Unless the diagnosis is quite clearly defined it should not be made In the greatest number of cases the therapeutic problem is primarily that of simple obesity and the principles involved apply to many of the cases due to endocrine disorder

The treatment of obesity logically requires the restriction of energy intake, as food, with or without taking measures to increase its expenditure, by exercise, or by other methods of raising the metabolism In our ordinary sedentary life, food restriction is most important and most effective The caloric value of the diet must be reduced to the point where the patient must draw on his body fats to meet his metabolic needs The cases shown here today are examples of the results to be obtained

when dietary restriction is pushed to a considerable length How the calories on such a restricted diet are to be best apportioned among the various foodstuffs is still a matter for debate The method employed in the two present cases has reduced the fat content of the diet to the absolute minimum This appears logical because the aim of treatment is obviously to force utilization of body fat reserves, and also because the caloric value of fat is greatest in the smallest bulk Bulk in the reducing diet must be made to substitute as far as possible for fuel value

TABLE 3

PERCENTAGE COMPOSITION OF FOODS CONTAINING PROTEINS OF HIGH NUTRITIVE VALUE, ILLUSTRATING THE CLOSE ASSOCIATION OF FAT WITH PROTEIN IN FOOD WHOSE PROTEIN CONTENT IS BIOLOGICALLY MOST VALUABLE

| | CHO | Protein | Fat |
|---|---|---|---|
| Eggs, whole | 0 | 13 | 11 |
| Cheese, Cottage | 0 | 29 | 36 |
| Cooked lean beef | 0 | 20 | 18 |
| Fish—salmon | 0 | 20 | 10 |

Since proteins of high value (milk, meat products, eggs) are usually accompanied by rather high proportions of fats, a certain amount of the latter is not to be avoided, and from recent experimental work, it is probable that total elimination of fat from the diet would be unwise even if it were possible It is wise on theoretical grounds to avoid wastage of body proteins, which means that sufficient must be given to keep the patient in nitrogen equilibrium Where the other foodstuffs are greatly reduced, however, their protein-sparing action is in a measure lost, and a higher percentage of protein than usual is then required for the purpose of maintaining the nitrogen balance Many reducing diets base the protein requirement on the "ideal" body weight It is probable that too strict use of the "ideal" weight as a measure for the protein requirement is as likely to error as is its inflexible use as a standard for other therapeutic purposes Despite past prejudices, there is no reason to suppose that restriction of protein intake below the minimal requirements for equilibrium, if practiced in moderation, will do harm As was shown above, both of these patients presented today were in negative balance

over considerable periods without injury or discomfort either at the time or after several months of subsequent observation

It is on the carbohydrate of the diet that we must rely for furnishing bulk and "roughage" The low and medium carbohydrate percentage vegetables and the fruits yielding the smallest number of calories with the greatest bulk furnish the major part of such a diet as was employed by these patients during their period of maximal restriction With such marked curtailment of diet it is best if the patient does not attempt to carry on his usual work, and observation in the hospital is indicated if possible, at least during the early period of restriction Many patients find that they can tolerate severe dietary restriction at rest but that this is impossible if they are obliged to carry on their usual labors, mental or physical Patients vary in their response to dietary restriction Acidosis under such circumstances is not common, but where a marked degree is present or where subjective symptoms are troublesome, additions of carbohydrate may be required After the first few days graded exercise, chiefly walking, is allowed Later the use of calisthenics or any other of the various types of light exercises may be employed if no complications are present The use of a cold shower or tub on arising is of assistance in stimulating metabolic activity

In most obesity diets reliance is to be placed on ample quantities of milk or its by products Milk has rightly the name of being one of the most nourishing of foods, containing necessary vitamins and mineral salts, but it should not be forgotten that it is also a comparatively dilute nutriment, and when the fat content is largely removed, as in skimmed milk or buttermilk, the caloric value is reduced by half A glass of whole milk (240 cc) has a caloric value of 163 calories, while a glass of buttermilk has but 86 and a glass of skimmed milk 67 calories Cottage cheese, made of skimmed milk, is another very useful by product

Diets as restricted in calories as these outlined can be made palatable and tolerable The influence of habit on food intake is nowhere better illustrated Such a 500 calorie diet permits the use of small portions of fruit, egg, and skimmed milk, or

breakfast food for breakfast, one or two daily portions of meat low in fat content (for example, chicken, shrimp, veal, or chicken liver, tuna fish, haddock, crab meat, oysters) ample quantities of 5 per cent vegetables, gelatin desserts, and milk The fuel value of certain commonly used vegetables is extremely low, as, for example, asparagus, canned string beans, lettuce, cucumbers cabbage, spinach, tomatoes, and turnips

No restriction of water intake is needed, and a plentiful supply may be of great assistance in preventing constipation The latter must be guarded against It is not necessary or advisable to restrict the intake of table salt unless there is the complication of an associated disease in which it may be indicated or unless the patient is in the habit of taking abnormally large quantities A large proportion of obese people without other obvious circulatory impairment suffer from swelling of legs or ankles which usually disappears with the general dietary treatment and without other specific therapy

Evans, upon whose general method the dietary treatment of these particular patients has been modelled, advocates the use of vitamin foods such as yeast, fruit juices, and fresh milk as well as careful attention to furnishing proper amounts of mineral salts We have paid careful attention to adequate vitamin administration through foodstuffs high in vitamin content Fresh fruits and milk if given in sufficient quantity will satisfy these needs, in combination with green vegetables of low caloric content We are rather conservative about the use of the various patent preparations for furnishing vitamins It has yet to be determined that they have any advantage over the natural foodstuffs, and we have seen troublesome abdominal distention with yeast preparations No one knows how well vitamin concentrates are absorbed from the human gastro-intestinal tract because they are always accompanied by other foods high in vitamin content

The rapidity with which weight reduction should be carried out is an unsettled question Nine or 10 pounds a month over a period of a year or more, as in the case of the first patient, can be removed without unusual discomfort from most persons

We believe that each case has to be decided on its own merits and on the general physical and mental response of the patient Marked physical weakness, tachycardia, insomnia and irritability of temperament are signs that the therapy is becoming too severe Under close observation in the hospital rather rapid reduction, as illustrated by these patients, is quite satisfactory, and a loss of 4 or 5 pounds a week may be sustained without untoward results over a considerable period The patient may then be discharged to ambulatory treatment on a more modified régime We believe in a large proportion of cases that rapid reduction on a greatly curtailed diet under hospital observation offers the quickest easiest, and most satisfactory way of obtaining the desired results

## CLINIC OF DR E W BRIDGMAN

THE JOHNS HOPKINS UNIVERSITY

### CORONARY OCCLUSION

THIS clinic is concerned with demonstrations of cases of coronary occlusion, examples of which have been collected partly from private practice, partly from a consultation service at the United States Marine Hospital in Baltimore They are presented with the purpose of accentuating various symptoms or signs that are characteristic of this condition, and, at the same time, with the intention of stressing the course rather than the diagnosis of this clinical entity

It would probably be of considerable satisfaction to Laennec, were he living in this laboratory age, to read of this relatively newly recognized sequel of coronary sclerosis, which has been clearly portrayed as a result of careful history taking and physical examination, checked by anatomical studies Certainly, it must be of great encouragement to those physicians who are primarily concerned with the practice of medicine, because it emphasizes the value of the patient's story and of physical diagnosis—methods of study that are easily slurred over since the x ray, for instance, has become so generally accessible

Most medical teachers of a generation ago grouped the cases of coronary occlusion under the generic heading—angina pectoris—and regarded as variations of that syndrome those examples that now constitute an individual and characteristic entity Two Russians, Obratzow and Strachesko, who published in the *Zeitschrift für klinische Medizin* in 1910, deserve the credit for the establishment of this clinical syndrome Herrick, in this country, soon followed, in 1912, with a similar publication in the *Journal of the American Medical Association* Since Columbus thus stood the egg on end, various and numerous

authors have described and discussed this condition so comprehensively, that today every text-book devotes space to its diagnosis, giving a picture as apparently simple and clear-cut as that of pneumonia or typhoid fever

I desire, therefore, to demonstrate to you several cases that bring up characteristic problems and to recount the stories of patients who have died, in order that you may, as it were, follow consecutively the completed histories of individual cases that have been followed over a period of several years

Case I—The first patient, here before you, C T M, a dentist, aged forty-five, came to the hospital February 24, 1931, and remained there for approximately four months His *complaint* on admission was "pain in my chest, left shoulder, and left arm" His *family history* was nonessential and there was nothing of interest in his *past history* beyond the fact that he had had influenza twenty years before We thought it important, however, that he smoked 30 cigarettes a day, was quite high strung, and had been doing extensive executive work, involving political difficulties, for the past several years

On the morning of February 13, 1931, he arose, and, after dressing, noticed a sensation of burning below the ensiform cartilage He had always been so perfectly well that he paid but little attention to it, although he took a little soda (without relief) A little later, as the discomfort persisted, he took milk of magnesia and obtained relief for a few hours There was a return of pain and burning later on, and he took considerable aspirin during the day That night, he had a heavy sweat, felt hot all over, and he thinks that he may have had some fever He, however, slept well that night, though during the next day he continued to feel much the same and complained also of salivation On the succeeding day the pain got worse, and apparently became localized over the precordium, it also radiated to the left shoulder and arm, after the first two days This pain was aggravated a great deal by exercise and was severe enough at night to keep him awake During the nights of February 18th and 19th he was compelled to sit up in a chair all night in

order to gain some relief, for as soon as he lay down the pain in the chest became unbearable He continued to work in the day time, but on the 21st, he felt particularly badly because of pain and burning By evening he felt quite well again and played cards after supper During the next two days he felt quite well, but on the evening of the 23rd after climbing stairs, he suffered precordial pain that was extremely severe, but it disappeared within an hour after going to bed, and he soon went to sleep He was awakened at 3 A. M on the morning of the 24th, with severe pain over the heart that radiated to the left shoulder This pain persisted and at times was so severe that morphine had to be administered, since it was not relieved by nitrites He reports that his blood pressure during this early morning attack was 138/100 He was brought to the Marine Hospital in Baltimore, where he was admitted On physical examination, there was evidence of pain (from his facial expression), and he had small pupils (morphine?) that reacted to light Mild chronic tonsillitis existed A soft systolic blow was audible over the apex, with otherwise normal cardiac findings No friction rub could be demonstrated His blood pressure was 128/94 He had rather hyperactive reflexes

His temperature on admission was normal, but on the next day it was 101 F , and during the following five days there was an average elevation to 99 5 F Thereafter, the temperature was normal or subnormal. His pulse rate, which was 96 on admission, gradually fell to an average of 74, after four days

During the first four days, he was kept in bed on a liquid diet and was given small doses of morphine, ¼ grain every four hours The pain finally completely disappeared, after having gradually decreased in intensity The morphine was correspondingly decreased in amount, with longer intervals between doses His stay in the hospital after the first two weeks was uneventful, his blood pressure averaging 124/80 At no time was a friction rub over the precordium demonstrable, nor was there any evidence of cardiac enlargement. The urine was not remarkable, and the Wassermann was negative The red cells, hemoglobin, differential count, and blood chemistry were quite normal On

admission he had a leukocytosis of 10,400, which gradually decreased, until, by the end of the first week, the white count was normal and so continued The *x*-ray examinations on admission revealed a heart of normal size and clear lungs, but an electrocardiogram taken three weeks after the onset showed definitely inverted T waves in the third lead, extending far below the iso-electric point, with an extremely quick take-off Several successive electrocardiograms showed a gradual decrease in the depth of the T waves until, after four months, the electrocardiogram became perfectly normal

The patient was given light massage after the second month, and before he left the hospital, he had been gradually able to increase his physical activity However, it was thought wise to continue his sick leave, so that there was a total period of seven months before he went back to active duty He was, of course, advised with regard to the stress and strain of life, was warned of the necessity of protection from overexertion, and was advised to give up the use of cigarettes

You see him today, four months after leaving the hospital, apparently perfectly well and he can now fulfill the demands of active duty However, he says he still has a little precordial sensation if he does too much A few days ago his electrocardiogram was perfectly normal, and there was no evidence of any cardiac enlargement, either on clinical or *x*-ray examination It would seem, then, that we have had to deal here with a rather small coronary thrombosis, which has left relatively little residual myocardial involvement—involvement that perhaps may be taken care of by the normal cardiac reserve There seems to be no question of the diagnosis in this patient, the continuous precordial pains (uninfluenced by nitrites), associated with a slight leukocytosis and fever, and with electrocardiographical evidence of myocardial disease are quite convincing

The therapeutic procedure for him consists mainly in the avoidance of the stresses and strains of life, and protection from overexertion One great difficulty lies in the fact that he is very restless and ambitious, slowing down will be a difficult problem for him!

Case II —Contrast the history just given with that of another person who died within a few hours after the onset of cardiac symptoms

A H B fifty two years old, was a lawyer engaged in active practice He was an extremely active individual and played squash several times a week His habits were excellent except that he smoked a package of cigarettes daily Beyond an occasional attack of tonsillitis, he remembers no day of illness One afternoon a few months ago, while walking home at the end of the day, he noticed some distress in his epigastrium that induced him to get on the bus and to ride uptown He had an engagement to go out to dinner that night, but he decided to stay home instead where he lay down without calling a physician By 9 o'clock, he felt so much better that he went to play cards at the house in which he had expected to dine After two hours still feeling perfectly well he called a taxi to go home While riding, he developed marked pain over his heart But he got out of the machine, and walked to his room at the Club without help, although he got into bed without undressing He called the physician who had seen him some two or three weeks before because of a recurrence of mild tonsillitis and because he had been wondering about the advisability of continuing squash At that time nothing had been demonstrated beyond the mild chronic tonsillitis and there had been some discussion about having his tonsils taken out The patient is quite certain that at that time there was no precordial distress, and no symptoms or signs of cardiac disease were elicited The blood pressure at that time, however, was 159/90 and it was on this account that the patient was advised to discontinue so active a game as squash

When I saw him on the night of the attack, two or three hours after the onset, he was mentally clear, but he had persistent precordial pain of a rather crushing character, that had been unaffected by nitrites, but which was eased by morphine There was very little radiation of the pain, according to his story, but he felt somewhat nauseated by it, and did not want to move because exertion aggravated the pain He was moderately prostrated, his face had a rather ashy hue and there was a little

cyanosis of his lips and ears Besides scarred but small tonsils and a little enlargement of his cervical lymph glands, he had a pulse rate of 96, a blood pressure of 100/60 (a contrast with that of two weeks before[1]) and there was slight elevation of temperature to 100 F His respiration was somewhat labored, but there were no signs of myocardial insufficiency—the bases of the lungs being clear, the liver not enlarged and the heart itself not enlarged on percussion There were no heart murmurs Near the base of the heart a definite, superficial friction rub was audible

He was kept very quiet for two hours and then, as there were no facilities for taking care of him at the Club, where he lived, it was thought wise to take him to the hospital On the way over in an ambulance, the pain, which had been pretty well controlled by morphine, increased steadily, and, suddenly, when in the elevator on a stretcher, on his way up to the ward, he developed what must have been from his expression, excruciating pain, clutched his heart, turned blue, and within a moment was dead No autopsy was done

Here again, one finds somewhat the same picture of preliminary precordial distress, followed by a sharp attack of pain uncontrolled by nitrites and eased by morphine, some elevation of temperature, tachycardia and, differing from the first case, a well-marked fall in blood pressure This fall in blood pressure is quite significant since it is the reverse of what generally happens in ordinary angina These findings plus the fever and friction rub make the diagnosis of coronary occlusion seem reasonable

The histories of these 2 patients bring out the difficulty of prognosis at the onset of the occlusion I saw both of these patients early and there was remarkably little difference in their clinical pictures The pain was somewhat more marked in the second patient, but he responded very well to small doses of morphine The degree of prostration seemed to be about the same, even when allowance was made for differences in temperament The fall in blood pressure in the second man was important, as was the early appearance of a friction rub However, the presence of pericardial friction is by no means constant in coronary occlusion, it depends upon the location of the resulting

infarct and especially upon its proximity to the anterior surface of the chest Often there is no pericarditis For me the essential lesson to be learned from these 2 cases was that where the diagnosis of coronary occlusion is suspected, it is futile at the time of the onset to try to guess the degree of heart damage All such cases merit complete rest, with morphine if necessary, the future course alone can decide the amount of damage done to the heart muscle

Case III —This next patient, W G aged forty five came to the Johns Hopkins Hospital for a check up one year after an attack of coronary thrombosis, and because of nervousness and depression He had always been a hard working individual and was consistently worried by his work which had to do with the production of moving pictures In 1928 he had had a nervous breakdown, the culmination of several years of nervousness, extreme depression and irritability Several times during the preceding year he had had crying spells and often would have to stop his work in the middle of the day and go home At that time he was seen by several physicians, one of whom finally persuaded him to give up work and to live a life of leisure, which he was financially able to do He had slight but definite signs of arteriosclerosis and it was believed that it was unwise for him to continue his emotional and worrying work.

One evening in February, 1929, while watching a prize fight, he felt somewhat nauseated cold and clammy, and became faint He was helped by smelling salts, but for several hours continued to feel uncomfortable There was no actual pain during this attack and by morning, he felt quite all right A week later, while at the race track, he had a similar attack, which was relieved by whisky A week later still, he was again at the race track and had a similar attack, which, however, was accompanied this time by a sense of pressure over the heart and sternum Whisky was tried without relief, and, as he thought the pressure was due to gas, he took some soda, which, however, increased the feeling of pressure and pain Doctors were sent for, and for about a week he was kept under opiates At the

time of this attack there was moderate dyspnea and persistent precordial pain, together with a low-grade fever He was kept in the hospital for a period of fourteen weeks His doctor reported that, besides the fever and pain, he had had a leukocytosis of 12,000 and definite electrocardiographical changes, but there had been no evidence of pericardial friction After leaving the hospital, he had had no pain or discomfort, but he had been extremely worried about himself and was constantly afraid that he might suddenly die He refused to be left alone and complained of a constant feeling of light-headedness and dizziness He admitted that he was "scared to death about himself" and thought that his present condition was the result of "nerves"

This patient was completely studied in the hospital, and the only cardiovascular findings of significance were those of the electrocardiogram, which showed a Q R S interval of 0 10 of a second, and an auriculoventricular conduction time of 0 20 of a second The T waves had suggestively quick take-offs It is fair, therefore, to assume that there had been some myocardial damage His a-ray film showed no cardiac enlargement, this was important because, sometimes, the late result of a thrombosis of a coronary vessel is a localized giving way of the ventricular wall with formation of an aneurysm of the heart Syphilis was ruled out by a Wassermann test of the blood and by studies of the cerebrospinal fluid The blood chemistry was normal and there was no evidence of renal involvement The eyegrounds showed a little distention of the veins where they were crossed by the arteries, and there was rather conspicuous streaking of the arteries, but without retinal exudation A psychiatrist who saw this patient felt, as I did, that there was evidence of rather early cerebral arteriosclerosis, particularly because of the condition of the retinal arteries, although the peripheral vessels and the aorta seemed to be normal

Believing that this patient has had a coronary thrombosis and that he now has some cerebral arteriosclerosis, we have to make the difficult decision with regard to the best possible therapy One feels that the residual involvement of the heart

muscle need not be considered too seriously the heart which has functioned fairly well for the period of two years since the coronary obstruction, ought to continue to do well in a reasonably protected life But this man has been so thoroughly scared about himself and is such an introspective person that it is not easy to reassure him Many efforts have been made to get this patient back to a reasonable mental attitude but he spends a good deal of his time going from doctor to doctor and his life is controlled by the fear of sudden death I have brought him before you in order that you may from now on keep in mind the abnormal mental states (especially in the form of "chronic invalid reaction") that may develop after coronary occlusion and to show you that in making a prognosis one must consider the philosophical outlook on life of the individual patient

Case IV —I have two more living patients to present to you, as well as a report of a patient no longer living The next patient is an example of coronary obstruction that has turned out to be relatively slight This man, R W W, forty three years old, an engineer by occupation, came into the Marine Hospital on the night of April 9, 1932, complaining of severe pain in his chest that ran down the left arm Except for influenza in 1918 and a neisserian infection in 1911, he had had, medically, an uneventful life He smoked two packages of cigarettes per day One sister had died of "kidney trouble"

On April 8th, about 9 30 P M, while undressing to go to bed, he developed sharp pain in the chest and inability to breathe In a few minutes he developed severe pain in the left arm A physician was called who gave him some medicine by mouth, at the end of three hours the pain had disappeared, and he went to sleep The next morning, he arose at the usual time without discomfort, and went to work At about noon, while still working, he had another severe attack of pain and was sent home by motor He was seen by another physician, who gave him two ampules of amyl nitrite that relieved him in a few minutes, but very quickly the pain reappeared, and he was carried to the hospital In the second attack the pain radiated down his left arm

and, on the way to the hospital, he developed pain in his right arm also After getting into bed in the hospital, he was much relieved by morphine, but some pain persisted and radiated down the left arm, especially into the little and ring fingers He was very conscious of having difficulty in breathing, because, he said, of pressure in his chest

On examination we saw a man rather old looking for his years, but well-developed and well-nourished His blood pressure was 148/92 No friction sound was audible and there was no cardiac enlargement For the first week his temperature varied between 99 and 100 F , the pulse rate between 90 and 110, and his respiration rate averaged 22 Thereafter, all three were normal The second day after admission, his blood pressure was 116/80 and a week later it was 90/50 No evidence of pericardial friction was ever made out and he responded satisfactorily to rest and to small doses of morphine After the third day, the pain was no longer constant and it gradually disappeared entirely, except for occasional twinges in his left arm After six weeks in bed, light massage was started and two weeks later he started getting up He was an extremely cooperative patient, relaxed quickly and was finally discharged after nine weeks in the hospital Examination of his urine and of his Wassermann reaction were negative His daily white count averaged 7000 His blood chemistry was normal during his stay in the hospital Several x-rays showed a heart that was consistently at the upper limit of normal in size The electrocardiogram, which was taken on the day after admission, showed waves of very low potential with atypical Q R S complexes together with a high take-off of the T wave in all three leads These same changes were evident five days later, but within a month there was nothing unusual to be made out by this method of study

A day or two ago, he was reexamined physically and no changes were noted, his heart was of the same size as before and an electrocardiographical tracing was within normal limits Since his discharge from the hospital, the patient has been working daily, and has taken very good care of himself He still has anginoid symptoms on undue exertion

Several electrocardiograms taken during the early period of his disease and at approximately monthly intervals since are here for inspection These tracings illustrate findings that are common in coronary occlusion—widening of the Q R S intervals, increase in the auriculoventricular conduction time, and quick take-offs of the T waves above the iso-electric point In the first patient that you saw, another common finding was shown, namely, a very deep and inverted T wave which, like these other changes, gradually disappears as the patient improves, though prone to vary in degree, even from day to day I do not believe that these changes in the electrocardiogram are positively diagnostic of coronary occlusion Rather, I would say that electrocardiography is a helpful laboratory procedure that may reveal evidences of impaired conduction secondary to diseased heart muscle tissue, but these same changes may be observed in persons with myocardial disease without previous coronary occlusion

**Case V**—I shall next read to you the history of a patient no longer living, a Mrs E C C, fifty-three years old, whom I sent into the Johns Hopkins Hospital the day I first saw her in her home She was then complaining of shortness of breath, nausea, high blood pressure, and dull pain in the right interscapular region She had had infrequent attacks of "heart trouble" for the preceding fifteen years, which were characterized by dyspnea, nausea, and fatigability With each attack she would go to bed for a few days, and would quickly recover Digitalis had been used at intervals during those fifteen years She had become rather accustomed to the attacks and had associated them with her high blood pressure that her doctor said had varied from 150 to 220 mm

She had had the usual childhood diseases, as well as influenza in 1918 from which she made an uneventful recovery Four years previously she had had several radiations for lichen planus with definite relief She gave a history of frequent colds and sore throats together with attacks of bronchitis She had had some heart consciousness but no actual pain, and some mod

erate shortness of breath during the so-called "heart attacks" There had been no edema at any time

She dated her illness as starting two months earlier while visiting in the Adirondacks She had begun to feel unusually tired and worn out, and her physician advised exercise and fresh air She said that she followed his advice but too strenuously, and suddenly became quite breathless and had to be put to bed She became nauseated and vomited at intervals for about ten days Thereafter, she temporarily improved, but suddenly, while taking a bath, she collapsed A physician was called and adrenalin was administered, which, it was claimed, saved her life She was kept in bed and given digitalis, food was forced In a few days she again felt better, and a week before consulting me she was motored to Baltimore by a friend After her arrival she had been continuously breathless, with a great deal of productive, irritating cough, and had been quite nauseated

When I saw her in her home, she showed moderate emaciation, sunken eyes, slight edema, and pallor of the mucous membranes The respirations were markedly increased and shallow, and she had to sit up on the side of the bed, in order to breathe at all The tonsils were adherent, there was a little pyorrhea The lungs showed some impairment of the percussion note over both lower fronts, but the percussion note was normal behind A few coarse râles were heard over the chest The heart was obviously enlarged, extending to the left anterior axillary line, with the apex in the sixth interspace, and dulness reaching 5 cm to the right of the midline The sounds at the base and the apex were muffled, but no friction sound or rumble could be made out The pulse rate was 104, with a blood pressure of 110/78 There was no evidence of pulsus alternans and the vessel walls were only moderately thickened The abdomen showed evidences of ascites and the liver edge extended a hand's breadth below the costal margin The spleen was not palpable There was slight edema of the extremities

She was sent to the hospital for further study, where her blood examination showed the hemoglobin to be 66 per cent, the red count 3,440,000, and the white count 11,400 The dif-

ferential count showed a normal partition of the white cells The nonprotein nitrogen was 46 mg , and the blood sugar was 110 mg per 100 cc The electrocardiogram except for the tachycardia, was perfectly normal showing Q R S intervals of 0 08 of a second, P-R time of 0 16 of a second normal take-off of the T waves and a rate of 100 per minute Her x rays showed a markedly enlarged heart with some diffuse infiltration of both lungs The urine was perfectly clear with a specific gravity of 1 022, and only an occasional white blood cell

Within twenty four hours her dyspnea had become much less marked as a result of rest and small doses of morphine Orthopnea again became a definite feature, however gradually increasing after the third day of hospitalization Evidences of bronchopneumonia appeared in the lungs, and the lung signs slowly increased, with spreading râles and increasing dulness, until, a week after admission, she died, apparently of myocardial decompensation associated with bronchopneumonia

On the day before death, her phthalein output was 45 per cent, the nonprotein nitrogen was 30 mg per 100 cc , and her urine showed no evidence of renal involvement Her blood pressure had been quite constantly low at 110/80 but that was thought to be the lowered pressure that one often finds after a long period of essential hypertension, when the heart fails This important clinical fact is to be remembered before discussing the autopsy findings At no time was there any precordial pain and the electrocardiogram was essentially normal!

The *autopsy* showed moderate chronic passive congestion of the viscera, with no evidence, either gross or microscopical, or any significant renal disease The important findings had to do with the cardiovascular system, in addition to well marked areas of bronchopneumonia that were scattered throughout the bases of both lungs There was moderate arteriosclerosis of the aorta with many pearly and calcified patches, some of which were broken and roughened The pericardium was adherent at the apex, over an area of 5 cm in diameter The heart was enormously enlarged in all diameters There was a peculiar projection of the anterior part of the apical region of the left

ventricle in the region of the adherent pericardium The left ventricle projected far beyond the tip of the right ventricle The tricuspid and mitral valves were delicate and not diseased The aortic valves were slightly stiffened and there were arteriosclerotic changes at the root of the aorta The left coronary artery was markedly sclerotic down to a point about the middle of the ventricle, where it was completely shut off by thick sclerotic placques This was confirmed by the microscope The whole apical portion of the left ventricle and the anterior part of the septum, together with a portion of the ventricular wall extending directly to the left from the septum, had become thinned out into a scarred wall, which was practically completely devoid of muscle This whole sac was filled up with a thrombus and soft necrotic material, which brought the surface of this diseased region up to the level of the surrounding heart muscle

It seemed astounding that this heart could have functioned at all, for, except for the endocardium and pericardium, the whole apical region of the left ventricle was a semifluid mass, aneurysmal in shape, which one would think should have ruptured long ago There was no rupture, and it was evident that one was dealing with an old coronary occlusion of some weeks' duration, secondary to localized arteriosclerosis of the left coronary artery, with a resulting infarct of the whole of the apex of the left ventricle This had undergone proteolysis and degenerative changes with resulting heart aneurysm, and had led to gradual myocardial insufficiency, which, in turn, had been followed by bronchopneumonia and death—and all this in spite of the fact that pain in the chest, left arm or neck had been repeatedly disavowed by the patient! One would think that if electrocardiographical changes were ever to be demonstrated during life, they should have been observable in this case Their absence confirms my impression that there is no electrocardiogram typical of coronary occlusion, by means of which one can definitely recognize the condition

**Case VI**—The last patient to be shown to you is D M F, a sixty-eight-year-old Irishman, who has long been a pharmacist

in the Public Health Service He entered the hospital on February 28, 1931, with what was regarded as a mild, acute upper respiratory infection

He had had pneumonia as a young man and what was probably typhoid fever in early adult life He had been in the hospital for a few weeks in 1925, when it was found that he had a moderate hypertension, and a compensated but slightly enlarged heart, without evidence of renal disease He had gone back to regular work and had experienced no difficulty until a few days ago, when he developed a cold with a rather annoying, slightly productive cough and some shortness of breath There was no pain in his chest beyond discomfort on coughing

On examination, the essential findings were tachypnea of 30, with scattered coarse râles in both lungs, a heart that was slightly enlarged but with clear sounds, and a blood pressure of 140/90 The pulse rate was 90 For twenty four hours he had slight elevation of temperature, averaging 100 F He was kept in bed for a week, and then allowed to get up and to increase his activity slowly At the end of the second week, however, without the knowledge of his doctor, he left the ward and went to his room on the second floor of one of the out buildings After climbing the stairs he became extremely short of breath and developed considerable precordial pain of a constrictive character In addition, his temperature, which had been normal for nearly two weeks, became elevated to 100 F and a leukocytosis of 12,000 was found together with a pulse rate of 110 He was not moved for twelve hours, but was then carried on a stretcher back to the ward, where, after a few days of absolute rest in bed, and ¼ grain of morphine at six hour intervals, the pain was controlled and gradually disappeared At no time was a friction rub definitely audible, although several observers mentioned a transitory scratchy sound that may have been evidence of some pericarditis

This patient has been kept in the hospital for nearly two years During that time there have been two similar attacks of precordial distress each of them associated with a little fever The possibility of repeated coronary occlusions has been kept in mind

The heart has gradually increased in size, but the enlargement has been diffuse and without evidence of local dilatation of an aneurysmal character In spite of great care and protection, there have been short periods of myocardial insufficiency and at times pulsus alternans has been observed

It is interesting to consider this patient from the point of view of one type of end-result following a coronary occlusion in a person who previously had had hypertensive cardiovascular disease Here the additional insult to a heart muscle that was already diseased has further limited the capability of the heart muscle, that is why this patient is constantly on the verge of myocardial insufficiency despite complete hospitalization with most of his time spent in bed (Here the patient was removed from the amphitheater) Obviously, the prognosis in such a patient is most unfavorable, we have to deal simply with a story of progressive cardiac failure All of that patient's electrocardiograms showed evidences of myocardial disease with increase of conduction time and malformation of the ventricular complexes The sudden increased destruction of considerable heart muscle tissue following infarction is, of course, of considerable significance in the history of progressive myocardial disease

Summary —It would seem, therefore, that there is a clinical syndrome, quite distinct from ordinary angina pectoris, which frequently develops in early old age and is especially apt to be associated with arteriosclerosis or with hypertensive cardiovascular disease It is astonishing how rarely, if ever, this condition is related to valvular or endocardial lesions It is interesting that commonly, even in previously healthy patients, there can be elicited a history of a period of a few hours or of a few days in which there had been prodromal symptoms (such as mild precordial distress or the sensation of abdominal distention) Subsequently, there commonly develops extreme precordial pain (that is not relieved by nitrites), dyspnea, and varying degrees of collapse

On examination, tachycardia, low blood pressure, pericardial friction, fever, and a leukocytosis may be found When cardiac enlargement is demonstrable, it is generally referable to some

preexisting cardiac disease Electrocardiographical changes may be present, which, although not pathognomonic of coronary occlusion are indicative of myocardial damage These electrocardiographical changes vary in degree in the same patient, from time to time, and are not necessarily indicative of the degree of cardiac damage

Whenever coronary occlusion is suspected, complete rest should be enjoined until all signs of acute distress have passed Even then, great caution should be observed during the gradual rehabilitation of the patient I do not believe it is ever possible at the onset of the disease, to appreciate, from the symptoms and signs, the extent of the subsequent infarction During the early stages of the disease, morphine is indicated, to control the pain and to permit the patient to rest Every effort should be made to keep the patient quiet, and to that end the ordinary routine orders embrace a simple liquid diet, the use of the bed pan, together with enemas every second day, if necessary Unless there be evidence of considerable myocardial insufficiency, digitalis is contraindicated There is evidence for the view that the chemical constituents of digitalis cause constriction of the coronary arteries, and except as a last resort where there is accompanying myocardial insufficiency of high grade, one should avoid its use The therapy should favor rest rather than increased exertion of the heart, we desire to avoid the breaking off of bits of thrombi, we wish to promote the healing of the diseased areas

In general, the prognosis in cases of coronary thrombosis depends upon the size of the area of infarction and the nature and extent of any previously existent cardiac disease With but a small infarction, the patient may recover and be able to resume a reasonably protected life, especially if he be mentally capable of avoiding overanxiety while at the same time bringing about the reorganization of his life that is necessary A second group of cases comprises those who die almost immediately, no matter what is done Those patients that recover from the acute attack but who have earlier had serious cardiac disease form a third group, they generally go gradually down hill, in spite of

of having recovered from the acute attack In these patients, as might have been expected, there is often a history of repeated infarctions There is a fifth small group of patients who though they recover from the acute attack and receive excellent care and protection, gradually develop aneurysmal changes in the heart muscle, followed sometimes by rupture

The diagnosis of coronary thrombosis is nowadays, as a rule, not difficult If one will look but for the well-known symptoms and signs of this condition, particularly in all cases of supposed angina pectoris, the correct diagnosis ought to be made in the majority of cases

BALTIMORE

## A CASE OF THROMBO-ANGIITIS OBLITERANS WITH FEATURES SUGGESTING AN INVOLVEMENT OF THE MESENTERIC VESSELS

THE case to be presented is of interest for several reasons In the first place, the symptoms and signs on the part of the extremities are typical of thrombo-angiitis obliterans, in the second place, there are abdominal signs and symptoms suggesting an unusual involvement of the mesenteric vessels in this inflammatory, thrombotic process, and in the third place, there are certain congenital defects or anomalies that serve to emphasize a probable, underlying constitutional factor in the etiology of this vascular disease

### CASE REPORT

The patient is a young man, thirty-one years old, of English and German parentage

His chief complaints (July, 1932) are of pain, numbness, and increasing disability of the left leg for about eighteen months One month ago after unusually excessive exercise he awakened one morning with the left foot cold, stiff and "dead" Since then there have been tingling and occasionally sharp stabbing pains in the left foot

The past history will be briefly summarized He is the elder of two children The parents are well, his birth was normal and he was a healthy baby, though rather fat to the age of six years or more During his early school days he would often read in preference to active play because he was apt to tire easily Later on however, at about twenty years of age, he enjoyed heavy work and marked physical activity on a ranch At

fifteen or sixteen there was a summer febrile illness that may have been typhoid fever He liked his sedentary work, was ambitious, and worked hard He took little exercise, smoked 20 cigarettes a day and took an occasional alcoholic drink

There has been no venereal disease and no surgical operation except the removal of the tonsils at fifteen

The present illness seems to have begun about three years ago with epigastric pain that came on at any time of the day and gradually resulted in a fear of eating, anorexia, and loss of weight There was no nausea, no vomiting, no diarrhea, nor constipation There was but little gas He became weaker or "lazier" and had to drive himself to do the day's work Medical examinations revealed a lack of acid in the stomach contents but no other evidence of an organic lesion within the abdomen He was advised to diminish the use of tobacco and increase out-of-door exercise Golf was tried but brought on great fatigue and attacks of abdominal pain Sometimes the epigastric pain was so severe that he would retire to another room, throw himself on the floor and beat it with his fists He formed the habit of keeping his hand beneath his belt and massaging the abdomen for relief Obvious functional nervous symptoms had developed and he was sent to a hospital for a general rest and upbuilding treatment He had been quite depressed but experienced a "glorious sense of relief to be able to rest," cooperated well and gained 25 pounds in one month

After leaving the hospital he spent two months of the spring of 1930 in the mountains, resting, reading, and engaging in other very mild activities Though he was bright, cheerful, and interested he had little physical energy and took no exercise He went back home and to work, remaining fairly well for four or five months Associated with increasing business worry there was a return of symptoms, epigastric pain, and what he described as a "generally rotten feeling in the stomach" He lost the weight he had gained and more besides

It was about this time, he thinks, in the summer of 1930, that he first had pain along the outside of the left thigh and into the left calf that came only with exercise There was increasing

disability in walking due to the pain in the leg There was a feeling of numbness and some weakness especially when the pain was present There were no cramps nor jerking nor twitching of the muscles

There was another period of one month in a hospital but it was much less successful than the previous one He gained no weight and was blue and depressed He went home quite miserable but gradually improved except for the increasing disability of the left leg

In the spring of 1932 he embarked upon a sea voyage through the Panama Canal with many stops along the coast There was marked improvement in spirits, in interests, and in appetite though he gained little or no weight He could walk about a mile with occasional stops to rest, during which if there were no seat available he would lean against a tree or post until the pain in the leg ceased

After the voyage was over, with some evidence of improvement he decided to push himself into more activity and on one day managed to walk four or five miles A few days later, early in June, 1932, he awoke one morning and found the left foot outside the covers, cold, numb, and "asleep" Rubbing and massaging the foot did not help At first he could not move ankle or toes but a great deal of power has returned Soon after this episode there began a tingling in the left foot and pain across the toes especially at night He has done little walking during the past month The pain in the stomach has been much less troublesome Indeed there has occurred only one sharp attack in three months and that lasted only a day or two He dreads the possibility of an attack and sometimes stops eating for fear of it even when he is hungry

**Physical Examination, July 7, 1932**—The patient is tall, quite thin, with fairly large bony framework and well marked facial acra He walks with a slight limp, favoring the left leg The complexion and hair are dark. His manner is pleasant He talks easily and freely and does not appear depressed

His height is 71½ inches, the weight 118½ pounds He is accordingly about 50 pounds underweight As he stands, the

pelvis is tilted, the right side higher than the left, the shoulders are level, there is a very slight lateral curvature of the spine, otherwise the spine is straight and its movements are very good As he lies on the couch there is no apparent shortening of the left leg but the left leg appears smaller than the right On measurements, from anterior superior spine to internal malleolus the left leg is 1 cm shorter than the right Bryant's line is 1 cm shorter on left than on right The circumference of the left thigh is 1 cm less than that of the right thigh and the left calf is measured 2 cm smaller in circumference than the right calf There is no enlargement of the joints of arms or legs and no limitation of their motion

The radial pulses are synchronous, of regular rhythm and good volume The rate is 80 per minute, blood pressure 120/75 The radial wall is not thickened nor is that of the brachial or temporal arteries The retinal arteries are not remarkable

The heart is apparently of normal size There are no pathologic shocks nor thrills The sounds are clear

The pulses in the femoral arteries are distinct and synchronous The popliteal pulse is felt on the right but not felt on the left No pulse can be detected in the posterior tibial or dorsalis pedis artery of either foot When the sphygmomanometer is applied to the legs, the oscillations of the needle are diminished on both sides, more markedly on the left There is no distinct difference in the surface temperature of the thighs nor of the upper third of the legs The skin over the left ankle is definitely cooler than that over the right and the left toes are quite cold The toe nails are ridged and slightly thickened, and the patient says they have shown little or no growth in length In the recumbent posture the color of the feet is about the same, when dependent the dusky color is more marked on the left and when elevated the left foot blanches more quickly and more completely than the right There is no edema There is no enlargement nor obvious disturbance of the veins

On neurological tests, the cranial nerves are normal Muscles of the arms are slender but strong, the grips are equally good, no muscular twitchings are seen Deep reflexes in the arms are

present and equal The muscles of the smaller left leg are flabby they react normally to faradic and galvanic stimuli, strength is reduced at ankle, knee and hip, more severely at distal joints The knee jerk and ankle jerk are distinctly exaggerated on the left and normal on the right There is no clonus and no Babinski The left abdominal reflex is much reduced, that on the right is active There is a moderate loss of all forms of cutaneous sensibility over the left toes and foot gradually fading out over the leg There is no tenderness, no loss of vibratory sense nor of sense of passive movements There is no ataxia The motor and sensory functions seem normal on the right

The mucous membranes are of good color, there is no jaundice. The cervical, axillary, and inguinal lymph nodes are palpable though small, the epitrochlears are not felt

The tongue is slightly coated The teeth are vital and of healthy appearance, the gums are normal The tonsils are not visible, the pharyngeal wall is red

The abdomen is symmetrical, its walls are soft, there is no tenderness The liver and spleen are not felt Quite deep in the right upper quadrant there is palpable a firm, rounded mass that descends on inspiration The lower edge of this structure is at the level of the umbilicus

The nose and sinuses are negative. The lungs are clear

The thyroid gland is not enlarged but is firm and slightly nodular There is no fine tremor of the fingers The skin is thin, smooth, and normally moist. The hair of the head is quite abundant, of medium texture There is a heavy beard and heavy eyebrows The trichosis of limbs and trunk is approximately normal Tests for latent tetany are negative The external genitalia are not remarkable The prostate is of normal size and consistency

Laboratory Examinations —*x Rays* —Roentgenoscopical examination of the chest shows a pendulous heart and moderately increased paramediastinal shadows

Roentgenoscopical and roentgenographical examination with barium meals reveal ptosis of the gastro-intestinal tract, spasticity of the colon and a filled and curled appendix

(The Graham dye test had previously indicated a normal gallbladder )

The paranasal sinuses are clear The sella turcica is of normal size

The thoracic spine shows slight evidence of arthritic changes in the upper portion The lumbar spine is negative The pelvic bones are not remarkable unless there may be a slight shortening of the neck of the left femur There is a rudimentary spina bifida over the lower sacral segments

There are no definite bony changes in the feet nor in the left leg in the region of the knee, and no calcification of the arteries

No abnormal shadows are seen in plain films of the kidney region After intravenous neoiopax, the pelves, calices, and ureters on both sides are well shown and indicate that the functional capacity is good and about the same on the two sides The arrangement of the shadows suggests a double pelvis on the right and perhaps also on the left The inclination of the calices at once suggested a horseshoe kidney to Dr H H Young who kindly examined the films The outline of the kidney substance is fairly well shown and is lower in position on the right than on the left A portion joining the two sides to complete the horseshoe is not definite

Other Laboratory Tests —*Basal Metabolic Rate* —The first period was minus 21 per cent, second period minus 19 per cent

*Gastric Analysis* —Free hydrochloric acid 8 acidity per cent, total acidity 16 acidity per cent, no blood

*Stool* —Normal, no blood

*Urine* —Entirely normal

*Blood Counts* —Red blood cells, 4,800,000, hemoglobin, 85 per cent, white blood cells, 6000, polymorphonuclear neutrophils, 58 4 per cent, polymorphonuclear eosinophils, 0 8 per cent, polymorphonuclear basophils, 0 4 per cent, small mononuclears, 35 6 per cent, large mononuclears, 4 8 per cent

*Blood Chemistry* —Sugar, 100 mg per cent, uric acid, 2 5 mg per cent, nonprotein nitrogen, 30 mg per cent

Total cholesterol of blood serum, 179 2 mg per cent, free cholesterol, 85 9 mg per cent, cholesterol esters 93 3 per cent, ratio of free cholesterol to cholesterol esters 1 08

**Special Tests of Circulation in the Legs**—(*a*) Neurovascular functional test of the left leg (This test was very kindly performed by Dr Ferdinand C Lee to whom we are deeply indebted.)

The skin temperatures of both legs were taken and showed that the left leg was about 1 2 C colder than the right, the greatest difference being 1 7 C on the skin of the great toe

The peroneal nerve of the left leg just back of the head of the fibula was then injected with procaine

Fifteen minutes after the injection there was complete paralysis of the muscles innervated by this nerve and the corresponding skin areas were also anesthetic to a greater or lesser degree, the area immediately above the external malleolus was completely anesthetic and the skin on the dorsum of the foot was almost completely so Temperature readings taken at that time showed that the dorsum of the left foot instead of being 1 0 C colder was now 0 6 C colder than the corresponding area on the right foot After thirty minutes the difference in temperature of the dorsum of the feet was about the same, 0 5 C

The impression obtained as a result of this test was that relaxation of the vascular tone by the blocking of the nerve caused only a very slight elevation of the skin temperature indicating that spastic phenomena played little or no part in impairing the circulation and that operations on the sympathetic nervous system offered little hope of improvement.

(*b*) The cutaneous histamine test

Intradermal injections of 0 1 cc of 1 1000 solution of histamine were made on the thighs, on the legs below the knees, just above the ankles and on the dorsum of the feet The tests indicated that the collateral circulation in the thighs was excellent and about equal on the two sides It was satisfactory below the right knee, somewhat less so below the left knee. The tests were weakly positive at right ankle and foot and almost nil on the left foot

Case Summary —In summary we have the following features

1 The arterial disease of the legs with history of intermittent claudication of the left leg for eighteen months and of a rather sudden occlusion of an important artery one month ago Pulsation in the left popliteal artery is not obvious and no arterial pulsation can be found in either foot There are temperature changes and color changes of the left foot and a feeling of numbness and of coldness with sharp pains in the left ankle and toes

2 The history of attacks of severe epigastric pain for three years with gastric hypoacidity and a spastic colon but no definite evidence of an organic lesion of the gastro-intestinal tract

3 Certain neurological changes in the diminution of the abdominal reflex on the left, increased deep reflexes of the left leg and hypothesthesia of all cutaneous modalities in the left foot, particularly the toes

4 Marked undernutrition by 50 pounds, a retarded basal metabolic rate of minus 20 per cent

5 The excessive use of tobacco

6 A reactive affective nervous disorder as shown by frequent depression, loss of interests, insomnia, fatigability and fear of eating

7 Certain structural anomalies, notably the slight shortening of the left leg with tilting of the pelvis, and the presence of a palpable deep mass in the right upper quadrant of the abdomen associated with x-ray findings suggestive of a horseshoe kidney

## DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of the arterial disease we must first consider whether we are dealing with an organic obstructive type or with a functional or vasomotor type of disturbance The case is plainly one of the organic obstructive type as shown by the steady persistence of symptoms and signs in contrast to the episodic nature of the phenomena in Raynaud's disease, by the lack of symmetry although both legs are involved in the process, by the persistent absence of pulsation in the peripheral arteries, by the excessive pallor with elevation and cyanosis in

the dependent position of the feet, by the history of intermittent claudication and by the presence of rest pain

In the further differentiation of organic types of arterial disease let us consider first the degenerative condition arterio sclerosis or endarteritis obliterans with or without thrombosis, second the inflammatory condition, thrombo-angiitis obliterans third, a number of less common conditions as for example em bolism for which we have no evidence, periarteritis nodosa a much rarer disease than those previously mentioned and usually with a distribution decidedly different from that shown in this patient In cases like the one just presented the differentiation lies between arteriosclerosis, on the one hand, and thrombo angiitis obliterans, on the other hand Although there are probably other types of occlusive peripheral arterial disease that do not fall exactly and typically into either of these di visions, not much is yet known about them and this rough classification must at present suffice. Most of the symptoms and signs enumerated above are common to both types of organic occlusive arterial disease and in differentiating between them we have chiefly the early age of onset of the symptoms and the roentgenographical appearance of the arteries with no evi dence of calcification, features that are characteristic of thrombo-angiitis obliterans, in contradistinction to the late age of onset and the extensive arterial calcification in arteriosclerotic disease

## FEATURES OF SPECIAL INTEREST

There are a number of features of special interest in this case, the discussion of which may at the same time bring out some of the characteristic and typical manifestations of the disease

**Constitutional Factors**—The etiology of this inflammatory, thrombotic lesion of the peripheral arteries (and in 30 per cent of the cases, of the veins) is unknown There are of course various hypotheses, for example, certain bacteria have been described in connection with the lesion, but the data so far are inconclusive and one cannot say whether it is an infectious disease or whether the lesion is inaugurated in some other way

than by infection There seem, however, to be very definite constitutional factors of predisposition to the disease One cannot say just how this predisposition is effected, whether there is a lack of resistance to a specific micro-organism, a generally defective arterial structure, a disturbance in the chemical equilibrium of the body, or a peculiar lack of resistance of the arteries to some definite damaging agent such as a micro-organism or poisonings from tobacco At any rate, the disease affects males almost exclusively Males of the Jewish race are much more susceptible than are those of other races For some time after Buerger's description the disease in 1908, with the increased interest aroused by his publication, there was a rather general opinion that the malady was confined to Hebrews Even today this impression prevails rather widely in the profession, although more recent statistics in different clinics where large numbers of cases have been observed indicate that while Jews make up a large proportion of the cases this large proportion constitutes only about 50 per cent of the total Cases have been described in men of practically all the European races, in Turks, in Chinese, Japanese, and Koreans In the history of our case there is no evidence, for at least three or four generations, of any admixture of Jewish blood

Of special interest in this case is the occurrence of other constitutional or developmental defects, features however that are not commonly reported in cases of thrombo-angiitis obliterans We have here the shortening of the left leg due apparently to a defect in the neck of the left femur, and also the deep abdominal mass with the roentgenographical evidence of a horseshoe kidney

**Exciting or Environmental Factors**—Our patient illustrates very well two of the very common and presumably quite important environmental or exciting factors of the disease, namely, the excessive use of tobacco and the marked exacerbation of the disease following unusual and excessive exertion Although the use of tobacco is not an invariable feature in the history of all patients with thrombo-angiitis obliterans, there is a strong impression among students of the disease that smoking is distinctly a dangerous habit for these patients Silbert states, in regard to

his treatment, that those patients who use tobacco do badly and those that stop smoking do well Barker analyzed the cases at the Mayo Clinic with this point in mind and found few non smokers in the series only 5 in 350 There were more excessive smokers than in a similar control series The cases in nonsmokers or in mild smokers tended to be mild and among the bad cases there were many heavy users of tobacco

**Course of the Disease and Distribution of Lesions**—Although many think only of a progressively downward course in thrombo angiitis obliterans, there may occur a spontaneous cessation of the pathologic process and permanent cure, and not infrequently there are spontaneous remissions and exacerbations of symptoms In our patient there has been a decided variation in the intensity of the abdominal symptoms but those of the legs had shown a progressively downward course until there occurred the sudden occlusion of an important artery about a month before we first saw him Since then, after a long rest and more intensive treatment in other ways, there has been distinct improvement in the circulation of the legs

The disease is characteristically one of the extremities, at least as far as the symptomatology is concerned In the statistics of all reported series of cases, the lower extremities are involved much more frequently than the upper extremities In Buerger's series of 100 cases the arms were affected in 21 He believes that the veins also are diseased in about 25 per cent of all cases The lesions, however are not confined to the vessels of the extremities Practically all of the arterial regions may be involved It is very difficult to form any satisfactory idea as to the frequency or the extent of such general distribution of the lesions in view of the fact that very few autopsies have been performed on cases with Buerger's disease The pathology of the vascular lesion has been thoroughly studied in the vessels of amputated limbs but Lemann, in the year 1928, could find the records of only 6 general autopsies

Taube, in 1931, being interested in the distribution of lesions found reports of 26 cases affecting other vessels than those of the extremities He decided that the disease may attack any

part of the vascular tree and that its distribution may be extensive In his table of the distribution of lesions the mesenteric arteries are listed twice, the celiac axis twice, the spermatic vessels twice, the renal arteries once, the aorta four times, the coronary arteries fourteen times, the cerebral arteries three times, and the iliac artery once

The first instance of mesenteric involvement was in the case of a girl reported by Buerger The patient developed intense abdominal pain and rigidity two days after the amputation of the left thigh for thrombo-angiitis The diagnosis of mesenteric thrombosis was made and at the operation a gangrenous intestine was found Meyer's case had had both legs amputated for thrombo-angiitis obliterans He had complained of abdominal pains, distension, and occasional vomiting of ten weeks' duration some time previously and finally had an acute gastro-intestinal attack accompanied by nausea, pain, and diarrhea At exploratory operation the transverse and ascending colon and all the loops of the small bowel were greatly distended The mesenteric vessels were sclerotic and no pulsation was obtained The patient died forty-eight hours after the operation No necropsy was obtained Taube then reports 2 cases of his own The first case was that of a Russian, forty-four years old, who had been under observation for several months with a typical bilateral involvement of the legs with a mild degree of gangrene During the second course of hospital treatment he complained of a dull abdominal pain with flatulence, vomiting, and general abdominal rigidity There was no distention nor tenderness The temperature was 100 2 F , pulse 98, white blood cells 20,000, of which 83 per cent were polymorphonuclear neutrophils The involvement of some mesenteric vessels was suspected The next day the temperature had risen to 102 F and on the third day was the same, the white blood cells 28,000 The condition subsided within a week and he was discharged free from abdominal symptoms About one month later a similar abdominal attack occurred and he was taken to another hospital There was marked abdominal rigidity and at operation 18 inches of gangrenous intestine were resected The patient died six hours

later The diagnosis was made of mesenteric thrombosis No postmortem examination was obtained Taube's second patient was an American Hebrew, thirty two years old who complained of severe epigastric pain He had suffered a similar but milder attack one year before The right leg had been amputated four years previously and the left leg removed a year afterwards with the diagnosis of thrombo-angiitis obliterans The severe epigastric pain was of several hours' duration and of agonizing intensity The patient threw himself about the bed pressing his fists into the epigastrium to obtain relief The abdomen was perfectly soft and deep pressure in the epigastrium or rubbing gave some relief He vomited several times The temperature was normal, the pulse 68, blood pressure 128/80 Three doses of morphine, $\frac{1}{4}$ grain each, did not alleviate the pain but two doses of atropine sulphate, $\frac{1}{150}$ grain each, relieved him considerably so that he slept for several hours The urine was normal, hemoglobin, 85 per cent, white blood cells, 9000, Wassermann reaction negative The abdominal pain was still present the following day but less severe On the third day there was slight soreness in the epigastrium and on the fourth day he was free from symptoms Two days later the roentgenographical examination after a barium meal was negative. Two months after this attack there was a similar episode that lasted ten hours Again six weeks later there was another attack of pain in the epigastrium with no abdominal tenderness nor rigidity and definite relief was obtained by pressure The temperature, pulse rate, and blood pressure were normal The patient's color was good He vomited once He would throw himself about in bed, rubbing and pressing his abdomen Two doses of atropine gave him relief There were three more similar attacks during the following forty-eight hours and each time atropine gave relief At the time of the report the patient was free from symptoms and doing his usual work

In the case of our patient there is, at least, a strong suspicion that the abdominal symptoms have been due to an involvement of the regional vessels in the inflammatory process of thrombo-angiitis obliterans During several periods of hospital observa

tion there has been no definite evidence of an organic lesion of the gallbladder, of the gastro-intestinal tract, or of the urinary tract and no abnormalities found except a gastric hypoacidity and some spasticity of the colon The attacks of abdominal pain were unaccompanied by fever or leukocytosis or abdominal rigidity and there was little or no abdominal tenderness While the pain is described as almost continuous in character, there were definite paroxysmal exacerbations of the pain that at times became so severe that the patient would retire to another room, throw himself down and beat his fists on the floor Distinct relief was obtained by pressure on the abdomen so that the patient formed the habit of keeping one hand beneath his belt and pressing over the epigastric region During his first period of hospital treatment, he experienced a pronounced relief at the prospect of rest and of freedom from the necessity of forcing himself to keep up with his daily duties There was at the same time a comparative relief from his abdominal distress He was able to eat satisfactorily and gained weight quickly The abdominal pain returned however some months later and was of similar character but not so severe as before During the period of our observation there has been no severe abdominal pain but not infrequently a sense of uneasiness in the epigastrium that affects the patient's appetite and his willingness to eat It would be impossible, of course, to differentiate these minor abdominal symptoms from those due to a purely functional nervous disturbance and the rapid and satisfactory relief from symptoms with marked gain in weight during his first rest cure certainly suggests a marked functional nervous participation in the causation of the earlier and more severe abdominal symptoms The nature and the degree of the abdominal pain however are quite unlike those usually seen in psychoneurotic patients It is interesting in this case that according to the history obtained from the patient and from his relatives, the abdominal symptoms antedated those in the legs This does not however determine the site of the original vascular lesion in view of the fact that it is not the presence of the inflammatory lesion but the extent of it and the ischemia produced that causes symptoms The in-

flammatory lesion may persist for some time before bringing about any marked change in the blood supply to the part

The signs of neurological disturbance elicited in our patient are unexplained While it is possible that they too may be related to the vascular disease, such an explanation is entirely conjectural It will be noted above that there have been reported cases of thrombo-angiitis obliterans in which there were features suggestive of involvement of the arteries supplying the central nervous system

Metabolism —Many of the victims of thrombo angiitis are very thin, almost to the point of emaciation like our patient and have been heavy smokers According to the studies of Silbert and Friedlander they have a low blood volume and an associated increase in some of the chemical blood constituents, notably in total protein, in calcium and cholesterol, but with a diminished phosphorus They found the chlorides and the sugar normal and the sugar tolerance normal These same observers find a uniformly low basal metabolic rate as in our patient and describe an increase in the blood volume with a return of the blood chemical figures to normal with the administration of thyroid tablets They also found a low rate of basal metabolism in apparently healthy, very thin young men who were heavy smokers

## PROGNOSIS AND THERAPY

There seems recently to have been a definite change in the attitude of the profession toward the prognosis and the therapy of peripheral arterial disease This may be noted in the American, in the British, in the French and in the German literature. There is much less of the former attitude of hopelessness and of the ready resort to amputation The change is probably due in part to definitely improved methods of therapy and in part to a better understanding of the diseases in question, with the recognition of spontaneous favorable changes in their course

Emphasis is now being placed upon the study of the physiology of the circulation in each case to determine how much of a vasospastic element there may be in a case of occlusive arterial disease or how much of an occlusive organic factor there may be

in a predominantly vasomotor malady The type of treatment in any individual case depends upon the outcome of such studies

The multiplicity of methods of treatment that have been devised and that are at present in use is indicative of the fact that none of them is altogether satisfactory or applicable to all cases We may summarize some of the principal methods of treatment of peripheral arterial disease as follows

METHODS OF TREATMENT OF PERIPHERAL ARTERIAL DISEASE

I General methods (rest upbuilding, sleep, occupational therapy, cessation from smoking, light massage, heat, careful protection of the part, postural exercises of Buerger)

II Special methods

(*A*) Those directed toward the vasomotor element

1 Injections of foreign protein (typhoid vaccine intravenously)
2 Periarterial sympathectomy
3 Lumbar or cervicothoracic neurectomy and ganglionectomy
4 The so-called "circulatory hormones" (lacarnol, padutin)
5 Vasodilating drugs
6 Irradiation of sympathetic ganglia or of peripheral arteries

(*B*) Efforts to increase blood volume and thus promote the formation and dilatation of collateral channels (Silbert's hypertonic sodium chloride solution intravenously)

(*C*) Alcohol injection of sensory nerves to relieve pain and to facilitate other methods of treatment

(*D*) Surgery of larger vessels

1 Ligation and section of main artery
2 Ligation and section of vein
3 Simultaneous ligation and section of artery and vein

III Amputation of diseased part

The general methods are those usually adopted and as a rule found helpful to some extent in any case of peripheral arterial disease A carefully worked out regimen of this type is considered by many observers as of the greatest importance and may account for some of the favorable changes ascribed in certain cases to some of the special methods of treatment The more important general methods are rest of the affected part, cessation from smoking or the use of tobacco in any form, and the postural exercises devised by Buerger General upbuilding and the promotion of sleep are made all the easier after some

improvement has occurred with relief of pain and anxiety Opinions differ in regard to the use of heat Some authors advocate contrast baths while other observers are afraid even of heat as for example, Schlesinger who says that each year he sees several cases in which in his opinion gangrene has been precipitated by the unwise application of heat

While spectacular results are not to be expected in cases of occlusive arterial disease, more rapid and satisfactory improvement has occurred after the use of therapeutic methods adapted toward the control of the vasomotor element in cases in which this is applicable Fortunately now there are several methods by which this factor may be tested The invention of the dermatherm or electric thermometer for the testing of skin temperatures has been very helpful

The injection of foreign protein, as for example, typhoid vaccine, in doses of 25,000,000 intravenously, is at once a test of the vasospastic factor in the case and a therapeutic method promoting the dilatation of the superficial vessels, a markedly increased blood flow, and an elevation of the skin temperature, provided these vessels are capable of such dilatation when the vasoconstrictor influences are removed

Other and simpler methods of determining the vasoconstrictor element in a case of occlusive arterial disease have been devised Scott and Morton, Eddy and Taylor, and others, by taking the skin temperatures with the dermatherm at different points of the body and extremities, have determined the vasoconstrictor gradient of the extremities, and what happens to it when the vasoconstrictor impulses are blocked both in the normal subject and in cases of peripheral vascular disease These impulses may be blocked by local or by spinal or by general anesthesia. In a normal subject or in a patient with a pure vasomotor spasm the temperature of the foot will rise 8 or 9 degrees centigrade, when the vasoconstrictor impulses are blocked. If the defect in the circulation is due entirely to an occlusive disease there will be no rise in temperature of the part after anesthesia is produced The various findings between these two extremes determine the relative importance of occlusive

and vasospastic features When vasoconstriction (or as some prefer to say, the lack of vasodilatation) is a prominent feature, then one of the special methods directed toward this vasomotor element may be chosen

The periarterial sympathectomy of Leriche has in the hands of most observers been evanescent in its effect and disappointing Bernheim believes that it may serve as a temporary expedient and that it sometimes aids in relieving pain

By far the most effective method of getting rid of the vasoconstrictor impulses to the lower extremities is by lumbar neurectomy and ganglionectomy Adson and Brown have reported a series of 100 patients with thrombo-angiitis obliterans so treated with quite favorable results They cite the relief of intermittent claudication and of rest pain in 85 per cent of the cases It is of course a major operation and to be undertaken only in carefully selected cases

The use of the ordinary vasodilating drugs has been disappointing Irradiation by radium or by x-ray has been used over the lumbar sympathetic and over the peripheral arteries themselves with favorable reports by several observers The method however has not met with favor in the hands of most students of the disease

The German literature contains a number of favorable reports on the use of the so-called "circulatory hormones" in cases of vascular disease both of the heart and of the extremities *Lacarnol* is an extract of heart muscle or voluntary muscle that is said to have a very favorable effect on many cases of angina pectoris probably through its action on the autonomic nervous system Its pharmacological action is perhaps based on the important ingredient, adenylic acid *Padutin*, formerly called *Kallikrein*, is said to be derived from the pancreas and to occur in large quantities in the urine, from which source it is obtained It is said that when the pancreas is removed the excretion of this substance in the urine ceases or occurs in minimal amounts Padutin is dispensed in ampules for injection in 1 cc quantity, intramuscularly, once or twice a day Very marked improvement has been described in thrombo-angiitis and in peripheral

arteriosclerosis by a number of observers after the injection of from 30 to 60 doses

In our case, we were led to believe by the result of the neuro vascular functional test that the circulatory defect was due almost entirely to an occlusive process and that but little was to be expected from an attack on the vasoconstrictor factor We have therefore instituted a therapeutic regimen based upon the general methods of treatment outlined above and upon another type of special therapeutic effort to increase the blood volume and thus promote the formation and the widening of collateral channels For this purpose we have adopted Silbert s method of injecting a hypertonic sodium chloride solution, 300 cc ot a 5 per cent solution, intravenously three times a week The administration of large amounts of fluid to patients with thrombo angiitis and the intravenous use of hypertonic citrate solution had been previously used Silbert chose sodium chloride because it is the salt to which the body is accustomed and because 15 Gm can be administered without danger of toxicity The hypertonicity was the feature desired and he did not look to the salt itself for therapeutic effect The solution is prepared in freshly distilled water, filtered and immediately sterilized For the first injection 150 cc are given and for all subsequent injections 300 cc Injections are given at first three times a week, and later twice a week, with the length of interval further increased as the patient improves It is given into a superficial vein in the usual manner by the gravity method, allowing it to run in slowly during ten or more minutes Unpleasant reaction did not occur For the purpose of establishing a standard for the rational judgment of the value of the treatment he made a study of the spontaneous course of thrombo-angiitis obliterans in a series of 250 untreated cases from the records of the Mt Sinai Hospital He found that 77 per cent of 155 patients required amputation of one extremity in a period of five years from the onset of symptoms In a series of over 200 cases treated by his method over a varying period of time of from one to five and a half years less than 10 per cent had required amputation and these 10 per cent were made up of cases whose condition was far advanced

when first seen He believes that with early treatment amputation would become a rare event The method seems to have been well tested and controlled by its originator Allowing for considerable enthusiasm on the part of the author of a method, one is still favorably impressed by its simplicity, its rationale, and by the results that he describes

After the thorough rest and upbuilding treatment with the cessation of rest pain and the appearance of other evidences of improved circulation, the importance of detailed care in the rehabilitation program is emphasized by Allen Precautions must be exercised particularly in the protection and care of the feet and of the nails, the selection of the proper shoe, the avoidance of cold, and the careful gradation of the amount of walking He permits his patients at first to walk for one minute in each hour, the remainder of the hour to be spent with the feet elevated on a level with the body This period of one minute may be gradually lengthened to five minutes in each hour before the patient is discharged from the hospital

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## CLINIC OF DR ERNEST H GAITHER

DIGESTIVE CLINIC, JOHNS HOPKINS HOSPITAL

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### PERFORATION OF THE ILEUM CASE WITH FOREIGN BODY FREE IN THE ABDOMINAL CAVITY

THIS case is presented for your consideration for two reasons First, such a condition is extremely rare, the literature as to perforation of the ileum has been thoroughly searched from 1731 to the present day, and only 3 other cases have been discovered which record a foreign body free in the abdominal cavity after perforation of the ileum The second reason possibly of even greater cogency, is the valuable experience obtained as to symptomatology, diagnosis and treatment in a study of this and other cases presenting a condition of such bizarre and atypical manifestations Such experiences should indelibly impress surgeons as well as internists with the exceeding significance of the ileum as a potential source of pathology, when evidence of intra-abdominal disease is presented, with a history of acute, subacute, or chronic disturbance

There have been recorded no subjective symptoms or objective signs particularly indicative or pathognomonic of this entity, and after a close perusal of the reported cases, we have found not one instance wherein the condition was definitely diagnosed preoperatively, or before autopsy

**Anamnesis**—A white girl, unmarried, eighteen years of age, complaining of severe pains in the lower epigastric and umbilical areas, these pains had prevented proper eating and sleeping, and patient states that she can scarcely walk when the pain is present The pain seems to bear no relation to food, either as an inciting cause, or as a relief from pain, it has not been of sufficient severity to require the use of hypodermic medication

The onset was about a month ago, it was very sudden, she did not pay any attention to it for a time, then she noticed that the attacks of pain came on at irregular intervals, were very severe, colicky in character, between attacks, however, she would feel quite well Diet, posture, season, exercise, played no rôle, and appetite was normal History entirely negative, other than the points enumerated

Physical Examination —A markedly undernourished girl, lying comfortably, quite pale The head, neck, and lungs were negative Heart not enlarged, slight roughening of the mitral and aortic firsts, moderate accentuation of the aortic and pulmonic seconds Blood pressure 115/0 Pulse 115 No thickening of the vessels, no general glandular enlargement In all other respects the body above the diaphragm was normal

*Abdomen* —A congenital visceroptotic type of lower thorax and costal angle, and scaphoid abdomen The lower pole of the right kidney was palpable, not tender or enlarged Spleen, liver, and left kidney not felt, the sigmoid was palpable and not tender The site of the pain and discomfort was across the whole abdomen immediately below the umbilicus During the first part of the investigation, the patient stated that the lower abdomen, both sides, was tender on pressure, when further pressure was applied, this tenderness disappeared, no tumor masses, muscle spasm, or visible peristalsis noted in the right lower quadrant Knee kicks active, no edema, normal tone to the somatic musculature Digital-rectal negative Weight, 98 pounds, normal, 123 pounds

*Sigmoidoscopic* —No evidence of ulceration, mucus, or growth, was distinct inflammation of the internal sphincter, in- al hemorrhoids

*Fluoroscopic* —Heart and lungs normal, stomach fish-hook in type, normal in size, tone, and peristalsis, no defect on either curvature, the greater curvature was three fingerbreadths below the level of the interiliac line The duodenum was normal The flexures were immediately above the interiliac line and the transverse colon in the bottom of the pelvis When the patient

was placed in the recumbent posture, the organs floated back to normal position

*Clinical Findings*—Test breakfast 24 and 56 Basal metabolism rate, minus 2 3 per cent Urine, several examinations were entirely negative Stool, negative microscopically, macroscopically, and for occult blood Blood Wassermann, negative, van den Bergh's, negative Differential count, normal Hemoglobin, 71 per cent White blood cells, 9900

Clinical Course—The symptoms continued as described above until an afternoon twenty six days after the first consultation The patient had walked in a leisurely manner several city blocks from her home when she was seized with an excruciating generalized abdominal pain She was seen within a half hour of the severe outbreak, lying on a couch bitterly complaining of severe generalized abdominal pain, the thighs were flexed upon the abdomen, and she was fearful of an abdominal examination Palpation revealed exquisite generalized abdominal pain and board like resistance, however, the tenderness was decidedly more marked in the lower right quadrant Active nausea and vomiting had ceased before my arrival Temperature 103 F Pulse 130 Respirations 28 Blood pressure 110/70 The skin showed marked pallor, but was not leaky, no dyspnea or cyanosis Urine yellow, cloudy, and specific gravity 1 019 Albumin, trace Sugar, negative Acetone, negative, diacetic acid, negative, casts, negative, pus cells, occasional Hemoglobin, 85 per cent Erythrocytes, 3,850,000 Leukocytes 20,000 Small lymphocytes, large lymphocytes, large mononuclears, 10 per cent Polynuclear neutrophils, 90 per cent

Diagnosis Ruptured appendix, peritonitis

Operation (within three hours of onset), Dr Alfred Ullman

On opening the abdomen, a large quantity of clear, straw colored fluid escaped, there presented itself in the incision a loop of brittle, stiff terminal ileum, with an open stigma at the apex of its curve, the loop being about 9 inches in length *A prune seed was found loose in the peritoneal cavity* There was no fibrinous exudate over the rest of the abdominal content The appendix was uninvolved Mesentery thick, hazy, and glazed in

the portion supplying the affected bowel The inflamed and ruptured ileum was excised and a lateral anastomosis was made between the cecum and ileum

Fig 201

Culture of abdominal fluid No growth

*Pathological Report*—Section of small gut measures about 30 cm in length The serosa is somewhat discolored, especially for two thirds of its length In this portion, there is marked

Fig 202

hemorrhage beneath the serosa and a portion of the mesentery adjacent to the bowel About 8 cm from the end there is a perforation through the wall of the gut which measures about

0 5 cm in diameter The discoloration is more marked at this point On palpation, the intestinal wall is markedly thickened, especially along the mesenteric side The mesentery is indurated, especially in the discolored portion as described above On opening the gut there is no normal mucosa present There is marked necrosis replacement with fibrinous deposits The wall itself is very edematous in the discolored portion, and particularly about the area of perforation, and just distal to this, there is almost complete occlusion of the lumen *Accompanying the specimen, is a prune seed which was found free in the abdominal cavity, this undoubtedly passed through the perforation*

*Microscopical Pathology*—Section taken from the distal end of the ileum in the neighborhood of the mesenteric attachment shows the tissue to be edematous There is very heavy white cell infiltration focal in character There is also a heavy polymorphonuclear neutrophil exudate present In the submucosa there is a similar white cell infiltration associated with polymorphonuclear neutrophil exudate, even more marked than on the exterior There is no mucosa present, but replacement by chronic granulation tissues and polymorphonuclear neutrophil exudate There is an area where there are numerous giant cells present There is, however, no tubercle formation The giant cells seem to be of the foreign body variety, and on the interior of many, there are some detritus and pigmented crystals present

*Diagnosis*—Recurrent acute enteritis, perforation of ileum by foreign body (prune seed) Patient made an excellent recovery

This remarkable case affords a salutary lesson as to the advisability of envisaging the ileum as a potential site of pathology, not only when atypical and bizarre symptoms are displayed, but also when the symptomatology is that indicative of more common pathologic conditions of the digestive tract, for it is unquestionably true that we are all prone to exclude very rare conditions from our consideration unless we have had some such enlightening experience as this case presents

Of the 3 other cases in the literature, the foreign body free in the abdominal cavity was found once at autopsy (Flower, 1860), and twice at operation One of the latter, a child of five operated

on in 1900 by Guinard, recovered, the other an adult Arab operated upon by Abadie in 1913, died seven days after operation In all 3 cases, bits of identifiable bone were found free in the abdominal cavity, after perforation of the ileum

Careful study of all available literature on this subject in French, German, English, and American journals since 1731 makes it evident that ulcerative lesions of the ileum are very prone to rupture, an added reason for meticulous care and painstaking investigation in every case presenting abdominal pain or other signs of disease in the digestive tract

Abdominal pain when generalized, and very particularly when localized in the right lower quadrant—suggests such varied etiologic factors as perforation by a foreign body simple ulcer trauma, spontaneous rupture, typhoid, ascarides nephritis diverticulum

Trauma.—It is of the greatest importance to emphasize the fact that a large number of cases showing perforated ileum after sudden severe blows, *showed no evidence whatever of external injury*, hence, when a patient complains of generalized abdominal pain, or lower right quadrant pain, following an injury, one must not allow himself to be influenced by an absence of external trauma, but depend upon a close study of subjective symptoms, objective signs, and results of clinical investigations, for a diagnosis, if doubt is entertained, after such thorough study, operation should not be delayed It will, I am sure, prove of value to present several interesting cases, the earliest record of traumatic perforation we found was published in Paris in 1731 by Christian Wolfius, and copied in the Philosophic Transactions, London, in 1732 "A strong laboring man was bruised by a stone falling on his lower belly, *he received no wound by this accident*, and died unexpectedly the next day, upon opening the abdomen there was found a great rupture in the ileum, so that it cohered with the rest only behind, the contents being poured forth into the cavity of the abdomen —From a livid spot in the abdomen, I concluded that the stone had fallen with its acute angle on the belly, and that the intestine was bursten by too great a tension, as bent bodies are broken on the upper convexity "

In 1866, Lane reported 2 cases (1) A healthy man seized during the night with sudden, generalized abdominal pain, vomiting, symptoms of peritonitis, exitus in two days, the patient had affirmed that while carrying a heavy burden he "felt as if something had given way inside" Section revealed a small perforated ulcer in the ileum, no signs of contusion or blow Lane believed that the powerful contraction of the abdominal muscles caused rupture of the ulcer (2) A thirty-four-year-old laborer, who, while carrying sacks of coal, "felt as if something gave way inside" Symptoms of peritonitis developed, an old right-sided hernia was repaired, being considered responsible for the symptoms, exitus in three days Autopsy, peritonitis Six inches above the opening into the large intestine, a small perforation in the ileum, on opening this part of the intestine, there was found an ulcer as large as a sixpence, ruptured in midportion, no involvement elsewhere

**Ulcus Simplex** —Grassmann, of the Munich Municipal Hospital, published in 1925 a study of simple ulcer of the ileum, in which he analyzed 51 cases culled from "world literature", only 31 cases fell directly under his definition of ulcus simplex, of these 31, perforation of the ileum occurred in only 15 The ulcers were various in size, the largest being about 2 cm in diameter, and the smallest pea-sized they were circular, elliptical, or oval, microscopically, 12 of them resembled chronic ulcer They were terrace or funnel shaped, tapering off, with all the characteristics of the classical gastric ulcer The edges were regular, clear, and thickened with heavy cartilage and a viscous infiltration In some cases, the ulcer had the appearance of being made with a bodkin or punch Of the cases, 25 were men, the largest number, 11, in the fifth decade, the youngest was a girl of seventeen, the oldest a woman of seventy-seven, occupations were various

It is interesting to note the diverse opinions as to etiology Some authors consider the possibility of precedent acute or chronic enteritis, and that there are intermediate stages between the so-called "catarrhal ulceration" and the ulcus simplex itself, others consider it may be due to inflammatory lesion from

trauma, foreign body, toxemia, infections etc and feel assured there is a connection between mechanical circulation and nervous disturbances, and again, there are those who think the infection theory the only valid one for small intestine ulcer

It has been asserted that ulcers of the upper small intestine are not peptic in nature, but probably derive from the fermentative influence of the pancreas, and are therefore tryptic Stuber (Münch med Wochenschr, 1914) showed by animal experimentation that tryptic ulcers in every way resembled acute and chronic ulcer, and the conclusion is drawn that trypsin plays an important rôle in the pathogenesis of intestinal ulcer it should be stated, however, that pathologically anatomically these ulcers display the characteristics of acute and chronic ulcer of the stomach and duodenum Johann Hofhauser (Arch Klin Chir, 1928) states that only 9 cases showing perforation of the small intestine have been noted in 16,000 operations in the last ten years, in the Surgical Clinic of the University of Budapest This author collected 54 authentic cases of ulcus simplex, of which 35 cases were perforation of the ileum, 58 per cent of the perforated cases that underwent operation, died, 28 per cent of all cases were cured

A vital question for consideration is that of the tendency toward stenosis in ulcerative lesions of the gastro-intestinal tract, Fuchs of the Hochenegg Clinic thinks it a rather frequent occurrence, König of Prague has seen it in but few cases, certain it is that stenosis must be included among the potentialities

Ulcus simplex occurs twice as often in the ileum as in the jejunum, it is usually found near the proximal portion of the mesentery, also in the free border of the intestinal wall, and it is to be noted that there is a decided tendency to early penetration, leading to generalized peritonitis Indeed, it has been asserted by some authorities that ileal ulceration develops without marked symptomatology, and that perforative peritonitis is as a rule the first indication

Tuberculosis of the Ileum.—H Reimann (Wien med Wochenschr, 1927) reports an interesting case of several possibly tuberculous ulcers of the ileum, of which one had perforated

Microscopical examination of the extirpated lymph glands showed recent tuberculosis, it was noteworthy that the history gave not the slightest indication of tuberculosis, and only the faintest apex dulness was found Lecène (Surgical Therapeutics) makes a most instructive statement regarding the course of tuberculous ulcers of the intestine "Most frequently, in the case of tuberculous ulcerations of the small intestine, there are adhesions between the loops, and the perforation is thus made into a neighboring loop, or into a portion of the peritoneum which is bound by adhesions, and in this way a pyostercoral abscess is formed, and a general peritonitis avoided" This same conclusion had been reached in 1878 by Spillman, and in 1895 by Barbe, and it is significant that the ever-increasing number of laparotomies performed for diffuse peritonitis does not seem to invalidate this classic opinion It is to be noted that while tuberculous perforations do occur, such a process is quite rare, and very few cases of perforation from uremia have been reported

**Latent Perforation.**—That single or multiple ulcers of the ileum show a marked disposition toward latency of symptoms is highly significant, for a most dangerous group is that consisting of cases of latent perforation Violent pain for several hours, followed by complete cessation of pain and absence of symptoms until fully developed indications of peritonitis suddenly and disastrously appear, is characteristic of this group, however, the symptoms are often incomplete and atypical, or masked by symptoms of concurrent affections, yet others simulate accidents such as hemorrhage and strangulation From these facts arises the difficulty or impossibility of definite diagnosis, in most instances it is already too late for successful treatment when the underlying cause has been identified Various authorities have asserted that when an abdominal emergency is presented, and prompt operation performed, the finding of a single rupture of the ileum means a favorable outcome in the majority of cases, on the other hand, the presence of multiple ruptures makes the prognosis practically hopeless

**Miscellaneous Causes of Perforation**—Several cases of perforation of the ileum by Ascaris lumbricoides have been described,

and cases have been found in which there were simultaneously existing gastric and small intestine ulcers this latter finding emphasizes the need for close observation of the intestine when operation is instituted for gastroduodenal ulceration

Treatment.—Of the highest importance is the decision as to necessity of surgical interference in order to forestall rupture, and local or generalized peritonitis No signs or symptoms specific of acute ileal inflammation, ulceration or perforation exist to aid us in differential diagnosis, but experience overwhelmingly verifies the urgency for early diagnosis, and immediate application of surgery with the most minute scrutiny of the ileum as the possible and probable site of disease

## SUMMARY

It would seem that valuable lessons may be learned from the case under discussion, and an intimate study of the recorded cases in literature

Attention should always be directed toward the ileum when symptoms of intra abdominal disease, either typical or atypical, are presented Consideration should also be given to the pos

## CHART

TYPES OF PERFORATION OF THE ILEUM IN COMPILATION OF 98 CASES

| | Cases. |
|---|---|
| Ulcus simplex | 31 |
| Trauma | 18 |
| Tuberculosis | 13 |
| Typhoid | 9 |
| Miscellaneous (nephritis etc ) | 9 |
| Spontaneous | 7 |
| Foreign body *not free* in the cavity | 6 |
| Foreign body *free* in the cavity | 3 |
| Ascaris lumbricoides | 2 |
| | 98 |

sibility of spontaneous rupture of latent ulcers by the contraction of abdominal muscles under stress and strain of carrying or lifting heavy burdens, and by no means must we be deceived

if, with a history of a severe blow in the abdomen, there is no external evidence of trauma

It is rather discouraging to note that in the cases studied there was in not a single instance a specific preoperative diagnosis of perforation of the ileum However, this should be a challenge to further diagnostic efforts on the part of radiologists, internists, and surgeons

The accompanying bibliography by no means covers all the references in literature to perforation of the ileum, but a sufficient number has been chosen to indicate the extreme rarity of cases such as our own, in which the foreign body was found free in the abdominal cavity

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# CLINIC OF DR. E. B. FREEMAN

GASTRO-INTESTINAL CLINIC, JOHNS HOPKINS HOSPITAL

## CHRONIC CARDIOSPASM

Etiology.—The condition which we now know as chronic cardiospasm was first described by Purton in 1821 as "Diffuse Dilatation of the Œsophagus without Obstruction at the Cardia." In 1878 Zenker and Von Ziemssen were able to collect 17 cases from the literature, they also reported 2 of their own. In 1888 Meltzer and Mikulicz, each working independent of the other, came to the conclusion that diffuse dilatation of the esophagus without organic obstruction at the cardia was due to chronic cardiospasm which resulted in retention of food in the esophagus with subsequent dilatation. This view was widely accepted and is the one generally held now. Two other views, however, are held at this time. One by Hurst, Rake, and others, that diffuse dilatation of the esophagus is not due to a spasmodic closure of the cardia, but to a lack of normal relaxation. Einhorn was the first to suggest that diffuse dilatation of the esophagus without organic obstruction was due to a lack of normal relaxation of the cardia during the act of swallowing. Under normal conditions, there is a momentary retention of food at the cardia before it enters the stomach. This fact has been definitely established by fluoroscopical study. Many years after Einhorn's suggestion Rolleston came to the same conclusion, but both Einhorn's and Rolleston's view, however, was passed unnoticed by the profession. Hurst, in 1915, again suggested that diffuse dilatation of the esophagus was not due to spasmodic closure of the cardia, but was really due to a lack of normal relaxation, and to which he applied the term "achalasia." The other view is that advanced by Mosher—that there is an organic basis for diffuse dilatation

of the esophagus, it being due either to pressure of the liver on the esophagus, or to a backward turn of the esophagus just before it enters the stomach, frequently, both causes acting together He further states that spasm can make a bad matter worse, but it does not originate the condition The posterior surface of the left lobe of the liver reinforces the front face of the terminal portion of the esophagus in the same manner that the cricoid cartilage stiffens the upper part of the esophagus Lateral webs and thin diaphragm-like stricture with a small central opening are characteristic of the upper part of the esophagus The same type of stricture is found in the liver tunnel back of the liver Mosher further states that most of the strictures which he has found in chronic cardiospasm are of these two types His findings, however, do not agree with most observers

Pathology —A review of the literature on chronic cardiospasm reveals the fact that very few pathologic studies have been made There are, I believe, two chief reasons for this The first is that chronic cardiospasm is a comparatively rare disease Vinson in a paper on the treatment of chronic cardiospasm reported a series of 683 cases from the Mayo Clinic When one considers the large number of patients studied at the Mayo Clinic every year, and that this number includes all cases of chronic cardiospasm presenting themselves for treatment from the time the clinic was organized, it readily becomes apparent that chronic cardiospasm is a rare condition In the digestive clinic of the Johns Hopkins Hospital from the time it was instituted in 1912, there have only been approximately 150 cases The second reason for the few complete pathologic reports is that chronic cardiospasm seldom proves fatal, and as no operative procedures are carried out for its relief, the only pathologic material available for study is that obtained from the rarely fatal case

I did find, however, one complete pathologic report by Mosher and McGregor, and also twelve complete reports by Geoffrey William Rake In 1924 Hurst expressed the opinion that the majority of cases of chronic cardiospasm were due to organic disease involving Auerbach's plexus Rake, acting upon Hurst s

suggestion began a very extensive pathologic study in cases of chronic cardiospasm to determine to what extent, if any, Auerbach's plexuses were actually involved in the pathologic process He made a careful microscopical study of sections made at different levels of the dilated esophagus and found that there was definite degeneration of Auerbach's plexus in all the cases examined He further states, however that this may not be true in every case A lesion of the vagus in any part of its course, provided it be bilateral, is able to produce nonrelaxation of the cardiac sphincter and loss of tone in the esophageal walls In the Mosher and McGregor case and in the 12 cases reported by Rake, there was no evidence of organic obstruction found at the cardia In a fatal case that I reported at the meeting of the Southern Medical Association in Birmingham, I was unable to find any gross evidence of organic obstruction at the cardia A microscopical study made by Dr L Clarence Cohn, failed to disclose the widespread degeneration of Auerbach's plexus as noted by Rake and by Mosher and McGregor, in that he found Auerbach's plexus well developed in the sections from the cardia and in sections taken a few centimeters above the cardia Sections also were taken from the stomach below the cardia, from the antrum of the stomach and from the pylorus Likewise, in these locations, Auerbach's plexuses were much in evidence

Symptomatology —The three chief symptoms are difficulty in swallowing, regurgitation or ejection of food from the esophagus, and pain beneath the lower end of the sternum or high up in the epigastric region The onset is usually sudden with a sensation of the food sticking beneath the lower end of the sternum This sensation, in the beginning, is usually of short duration There may be no return of this symptom for days, and in some cases, even weeks With each return, the distress beneath the lower end of the sternum becomes more marked and lasts longer, and sooner or later, the patient learns to obtain relief by voluntarily emptying the esophagus. The attacks increase in frequency until finally the patient is unable to eat a meal in comfort. The substernal distress at this time may amount to severe pain and may be constantly present. The ejected

esophageal contents is usually alkaline in reaction and consists of undigested food mixed with a large quantity of mucus and some salivary secretion The patient learns to eat very slowly, and, as the disease progresses, frequently chooses food of liquid and soft consistency, which sometimes results in an unbalanced diet Therefore, occasionally, these patients present the clinical picture of a high-grade secondary anemia with splenic enlargement Some patients find by drinking two or three glasses of water with their meal, and by making special muscular efforts at swallowing they are able to force a considerable quantity of their food through the cardia Also, some patients find by sitting in the erect position and by breathing very deeply, the food passes into the stomach more freely There is no doubt that certain articles of food in some cases do seem to precipitate an attack Many patients state they can bring on an attack by hurriedly swallowing a few mouthfuls of ice cold water

Usually, after the onset of the disease, there is a very definite loss in weight, but after the disease is once established, the weight remains constant at a lower level Patients are usually able to carry on their regular vocation providing it does not entail severe muscular exertion Regurgitation of food is quite a frequent occurrence during sleep In the well-developed case, the esophagus is never completely empty, always containing a considerable amount of undigested food, mucus and other secretions In the recumbent position, during sleep, the esophageal contents is likely to regurgitate into the pharynx and thus gain entrance into the larynx, resulting in severe paroxysms of coughing In a small group of cases, the obstruction at the cardia is almost complete, resulting in huge dilatation of the esophagus, as much as 2000 cc of contents having been aspirated Increased salivation, so frequently stressed by some English authorities, has not been a prominent symptom in the cases that have come under my observation

Pain of varying degree is frequently associated with cardiospasm Sometimes it is merely described as a discomfort or a pressure-like sensation beneath the lower end of the sternum, but in about 25 per cent of the cases the pain is quite severe,

Fig. 203.—Film showing whole esophagus of case reported. Diffuse dilatation. Regular outline cardiospasm.

diagnosis is quite difficult to make. In some attacks of severe pain, the patients complain that it radiates through to the back, which is again confusing from a diagnostic standpoint. These severe attacks many times require an anodyne for relief. A small percentage of patients suffering with chronic cardiospasm complain of shortness of breath after exertion and also at night. With the shortness of breath there is a pressure sensation in the

substernal region These symptoms, of course, are most likely to occur in patients who have a huge esophagus in which a large quantity of food and esophageal secretion is constantly retained

**Diagnosis**—The diagnosis of chronic cardiospasm is relatively easy to make There are only two organic diseases with similar symptoms that might be confused with it, namely carcinoma at the lower end of the esophagus, and carcinoma of

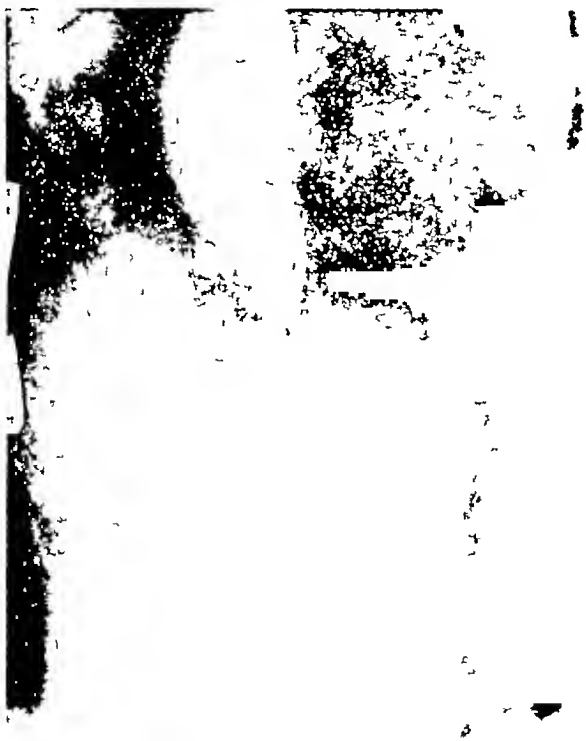

Fig 204—Detail of the lower end of esophagus shown in Fig 203

ie cardiac end of the stomach In both of these conditions, there is very little dilatation of the esophagus as compared with that found in chronic cardiospasm Some authorities state that the diagnosis can easily be made by a-ray alone This is true in many cases, but in the cases that are seen early, in which there is only moderate dilatation, two other methods of study, namely esophagoscopy and the passage of esophageal bougies, are neces-

Fig 205.—Detail of the lower end of the esophagus in a case of carcinoma of the lower third as contrasted with the appearance in cardiospasm.

hand, slight dilatation with marked irregularity in outline speaks just as forcefully for the lesion being carcinoma In both these conditions, however, the $x$ ray findings may be misleading in that carcinoma may be found in the lower end of the esophagus even though the esophageal wall seems to be smooth and regular Conversely, an irregularity in outline may be found in chronic

cardiospasm These atypical findings are usually due to one of two conditions, namely food residue in the lower end of the esophagus, or malignant disease in the cardiac end of the stomach

While the diagnosis can be made readily in many cases by x-ray study alone, there still remains, however, a small group in which a more accurate procedure is necessary It is in this group that esophagoscopy is so valuable It is true that this procedure is quite difficult and requires special training, yet the fact remains that the results are by far more accurate It can be done in a well-equipped office or the out-patient department of any well-organized hospital It does not require hospitalization In fact, it is a routine examination in the Gastrointestinal Clinic of the Out-patient Department of the Johns Hopkins Hospital in all cases that present esophageal symptoms By this method, one can carefully inspect the walls of the esophagus and study any lesion that may be present Under normal conditions, the mucous membrane in the esophagus is pink in color and of soft velvet-like consistency In chronic cardiospasm, the mucosa is usually grayish in appearance and may show many superficial abrasions Ulceration is not a part of the disease and the presence of scar tissue is seldom noted If an ulcer of any size is noted, it at once brings up the question of malignancy Likewise, if an ulcerative lesion is found, its size and position can be determined, and if desired, a specimen may be removed for microscopical study After all, actually seeing the pathologic lesion under consideration, is by far more convincing than any indirect method of procedure can every hope to be

The passage of bougies determines whether or not an obstructive lesion is present If present, it determines the site of the obstruction and something concerning its nature There is absolutely no danger in passing bougies providing they are passed over a previously swallowed thread If a sufficient amount of thread has been swallowed previously and time allowed for it to become firmly anchored in the small intestine, it will act as a guide and make the passage of bougies a very simple procedure This, I believe, is the most helpful method we have at our command to determine whether or not we are simply dealing

with a spasmodic closure of the cardia or with organic obstruction This procedure is also very helpful in the differential diagnosis between chronic cardiospasm and organic obstruction at the cardia In chronic cardiospasm one is able to pass without difficulty a No 60 olive tipped French scale bougie, whereas, in malignant disease, one is very frequently unable to pass even a small sized bougie

Treatment —While cardiospasm as a clinical entity has been recognized for many years, yet as Vinson has so well stated, there is still a striking lack of uniformity in the procedures advocated for its relief However, those who are especially interested in diseases of the esophagus agree that some form of stretching or dilatation of the cardia is necessary to relieve the condition. Many different methods of dilatation have been advised Hurst, Rake and other English investigators believe the best method of procedure is to use a mercury filled esophageal bougie The bougies are made in different sizes and each contains 1 pound and 5 ounces of mercury When the bougie is introduced into the esophagus its weight carries it down through the cardia This procedure has given good results in many cases, but apparently must be used almost daily—and even in some cases before every meal, to keep the cardia sufficiently dilated to permit the patient to take food in the normal way Rake however, reports one case who sought treatment the first day symptoms occurred, in which one treatment gave complete relief It would seem, however, that in a case that was treated the very day that symptoms occurred, there would necessarily arise some question as to the correctness of the diagnosis Other observers, particularly in this country, believe that the best method of dilatation is to pass bougies through the esophagoscope or to use some other form of a mechanical divulsor, likewise passed through the esophagus Still others believe the best way to produce sufficient dilatation of the cardiac sphincter is by passing large bougies over a previously swallowed thread as a guide, and if relief is not obtained by this procedure, to use hydrostatic dilatation Vinson reports very satisfactory results in some cases by dilating the cardia with a No 60 olive-tipped

French scale bougie passed in this manner He has been u this procedure for a number of years, and in the cases tha not relieved, he continues the treatment by using hydros dilatations In the clinic we have been using the No 60 bo in all cases, first, to determine if there is evidence of org obstruction at the lower end of the esophagus, and secon see how much relief may be obtained in this manner befor consider the use of the Plummer hydrostatic dilator If hydrostatic dilator is used, it is passed over a previously swallo thread in the same manner as the No 60 bougie We do however, use water to distend the apparatus, but prefe distention, which we believe gives just as satisfactory re and is a somewhat easier procedure In fact, we have used water to distend the apparatus for more than twenty y This procedure has proved very satisfactory in the great maj of cases I do not attempt to produce complete dilatatio the first treatment, but prefer to work the dilatation up gradu by slowly increasing the pressure in the apparatus with successive treatment I practically never use pressure gre than the equivalent of a column of water 15 to 20 feet in he In an average case, I give five or six treatments, I have, howe been able to give complete relief in a considerable percenta cases with one dilatation only

The question of giving these treatments under fluoroscop control has been discussed to some extent recently in the li ture Fifteen years ago I gave these treatments under flu scopical control I believe, however, that this is entirely necessary, and that if one has had sufficient experienc introducing the hydrostatic dilator, they should be able to p it quite accurately without the aid of the fluoroscope Ag to do this under fluoroscopical control necessitates working dark room, and personally, I very much prefer to watch my tient carefully while the dilatation is being done I always the dilatation if the patient complains of very much pain, then go on more slowly with the subsequent dilatations that be necessary to relieve the condition This method has l most satisfactory, and I believe gives a better degree of dil

tion than can be obtained either with the mercury bougie or by dilatation with bougies through the esophagoscope

In a small group of cases that are far advanced and markedly dehydrated it may be necessary to do a gastrostomy and dilate from below Vinson reports three such cases We have had one case recently in which a gastrostomy was done in a desperately ill patient—primarily for feeding purposes and subsequently for the treatment of the condition This patient however was so desperately ill that no attempt was made to dilate from below at the time of the gastrostomy—she died a few days later even though she was given a large quantity of food and frequent blood transfusions

The administration of drugs has proved singularly disappointing in my hands in the management of this condition Antispasmodic drugs such as hyoscyamus, bromide, and belladonna are helpful in relieving the associated nervous disturbances Chronic cardiospasm is not a functional neurosis—it is a definite clinical entity, and the use of antispasmodic drugs and nervous sedatives, or psychotherapy, are all disappointing as therapeutic agents

Although there is an associated esophagitis in all cases of chronic cardiospasm, it does not as a rule require local treatment through the esophagoscope as suggested by some observers As soon as the cardia is sufficiently stretched to permit the esophageal contents to enter the stomach freely, the esophagitis disappears In a small group of cases, particularly in the beginning of the treatment before sufficient dilatation has been obtained, washing out of the esophagus at bedtime is of some value By doing this, the esophagus is kept empty throughout the night and the disagreeable burning sensation sometimes complained of beneath the lower end of the sternum is relieved, which permits the patient to obtain a better night's rest

It is seldom necessary to do any sort of an operation to relieve the condition Three types of operation, however, have been performed, Mikulicz was the first to advise gastrostomy and stretching of the cardia from below This procedure was followed by rupture of the esophagus in a few cases, and for that

reason became unpopular Walton recently has recommended the same operation and has treated 14 cases in this manner, with only one fatality Heller in 1914 made a longitudinal incision through the muscular wall of the esophagus, the operation being analogous to Rammstedt's for congenital pyloric stenosis He collected 16 cases, in which the operation was performed with good results in 12 and no mortality Exner in 1917 performed an anastomosis between the abdominal esophagus and the stomach, and more recently, Turner has performed this operation on 2 of his patients Vinson reported 2 cases recently, in which the stomach was opened and dilatation made from below, with very satisfactory results

**Case Report**—S E, white, female, aged sixty years Entered the Gastro-intestinal Clinic of the Out-patient Department of the Johns Hopkins Hospital on July 24, 1931

*Past History*—Essentially negative except for a mild hemiplegia five years ago, which confined the patient to bed for ten days Before the hemiplegia there were frequent headaches, but none since

*Present Illness*—Began with difficulty in swallowing fifteen months ago associated with which there was a sensation as though the food was lodging beneath the lower end of the sternum In the beginning, the attacks were all of short duration The symptoms would occur with every meal for a period of two or three days, after which, there would be a remission of symptoms for several days At no time, however, from the onset of the illness, was there freedom from symptoms for more than ten days at any one time As the condition progressed, difficulty in swallowing and substernal pain was always experienced when any attempt was made to take food The pain became so severe that on four occasions it was necessary to give morphine for relief Regurgitation or ejection of esophageal contents was present from the onset of symptoms This is rather unusual in that these symptoms do not, as a rule, occur until the disease is quite well established When the patient entered the clinic she was having great difficulty in swallowing, severe pain beneath the lower end of the sternum, and was greatly emaciated The difficulty in

swallowing was so marked that on attempting to eat an ordinary meal she was forced to leave the table three or four times to relieve the substernal pressure and pain This she could always do by voluntarily ejecting the esophageal content At the onset of symptoms, her weight was 169 pounds but when she presented herself for treatment, she weighed 87 pounds only

*Physical Examination*—Showed a thin emaciated looking middle aged, white woman Skin dry Lungs clear to auscultation and percussion Heart normal size, sounds clear at the base and apex Blood pressure 160/100 No abdominal tenderness, no masses Liver, spleen, and kidneys not palpable Extremities normal, deep reflexes active Urine negative Wassermann negative. Blood picture normal

*Special Examination*—1 *x* Ray study showed the esophagus dilated, smooth, and regular throughout its entire length There is some evidence of obstruction at the cardia probably due to a neoplasm at the cardiac end of the stomach The *x* ray findings, however, were not confirmed by other diagnostic procedures

2 An olive tipped French scale bougie No 45 was passed over a previously swallowed thread, and no obstruction at the cardia was noted

3 Esophagoscopical examination showed the esophagus to be markedly dilated the mucous membrane grayish in color, and only a few superficial abrasions No organic obstruction at the cardia was found, as evidenced by the fact that a 10 mm esophagoscope entered the stomach without difficulty

Treatment was begun by passing a No 45 bougie over a previously swallowed thread twice a week After the fourth treatment the size of the bougie was increased to a No 60, this was found to pass through the cardia without difficulty, and after the third treatment, was discontinued Further treatment was then continued with the Plummer hydrostatic dilator, air being used instead of water to distend the apparatus The dilator was passed over a previously swallowed thread in the same manner as the bougies Six treatments were given, resulting in almost complete relief from symptoms In none of these treat-

ments was the pressure in the apparatus greater than that equivalent to a column of water 10 feet in height It has been now more than six months since the last treatment—there has been a gain of 34 pounds in weight and no return of symptoms

**Conclusions**—1 The etiology of chronic cardiospasm still remains undetermined

2 Careful pathologic studies made in the past few years indicate that there is a close relation existing between degeneration of Auerbach's plexus and chronic cardiospasm

3 The diagnosis can easily be made by *x*-ray examination, but in a small group it is necessary also to pass bougies and do esophagoscopy before arriving at a diagnosis

4 The best results in treatment are obtained by stretching the cardia in one of a number of different ways Personally, however, I prefer using the Plummer hydrostatic dilator, using air instead of water to distend the apparatus

5 Medical treatment gives no relief in these cases further than it relieves the associated nervous symptoms

6 There is apparently no justification for local treatment through an esophagoscope for the associated esophagitis

7 It is only necessary in the exceptional case to resort to any operative procedure for relief of the condition

## CLINIC OF DR CHARLES METCALFF BYRNES

JOHNS HOPKINS UNIVERSITY

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### TRIGEMINAL NEURALGIA

PAIN in the head or face is one of the most common affections met with in medical practice, but there are a great many painful affections in this domain which are not of the neuralgic type It is well, therefore, at the outset to understand clearly what is meant by neuralgia, and especially that particular form, to which your attention is directed, known as major trigeminal neuralgia or Fothergill's painful affection of the face

Neuralgia means nerve pain, neuritis, inflammation of a nerve Both are painful, but each has its distinguishing features In neuralgia, pain is the only symptom and it is intermittent, paroxysmal, darting, lightning like in character It is of short duration and directed along the course of a nerve trunk The pain in neuritis is often continuous, but variable in intensity, or even subsides for the greater part of the day, when, toward evening, it gradually increases in intensity and, at its height, may become neuralgia like in character Generally, the pain is said to be diffuse, deeply seated, of a dull, aching or throbbing nature, or described as a sense of soreness throughout the affected part There are, in addition, nerve tenderness and frequently objective sensory changes in the cutaneous field of the diseased nerve It is surprising how commonly these milder neuritic affections of the trigeminal nerve consequent upon sinus infection, apical abscess, a common cold or a neurosis are designated both by the laity and the profession as "neuralgia" of the fifth nerve

Having decided, then, that the patient is actually suffering from neuralgic attacks it must next be determined whether the

paroxysms are merely incidental in the course of a mild inflammatory process or truly of the major neuralgic type described by Fothergill The distinction is not difficult Major neuralgia exhibits certain characteristics which, at once, separate it from all other neuralgia-like affections of the trigeminal area, and I hope that the account of the following case, selected from my personal records of over 500 patients suffering from this disease, might furnish a helpful diagnostic picture of the disorder The record of one patient will suffice, since the character of the affection is identical in all of them It differs only in the age and sex of the patient, the side of the face affected, and the number of branches involved

**Case Report**—The patient, M V G, a woman, sixty-one years of age, was referred to me April 1, 1923, because of "pain in the right side of the face, mostly in the lower jaw" No one in her family had had a similar disorder, and her health previous to the onset of the face pain had always been unusually good

*Present Illness*—The first attack occurred suddenly in July, 1921, as a sharp, shooting pain which appeared to radiate from the second bicuspid tooth in the right lower jaw to the ear and chin of this side The pain was of momentary duration, when it disappeared completely and as suddenly as it had begun There were no further attacks for a period of two months, when paroxysms of the same stabbing character recurred in the original location They were again of *short* duration and followed by *perfectly free* intervals, but now continued for several hours almost daily All teeth in the right lower jaw were then extracted without affording any relief and, a month later, the "castor-oil treatment" was administered for two weeks with equally unsatisfactory result

In the latter part of November, 1921, Dr F made a deep injection of alcohol into the mandibular nerve This gave complete relief until the early part of December, 1922—a period of about twelve months—when, upon return of pain, two impacted wisdom teeth in the right upper and lower jaws respectively were extracted, but the paroxysms continued In February, 1923, Dr F made an unsuccessful effort to reinject the

mandibular nerve, and the attacks, still confined to the original location, persisted with increasing frequency and severity The patient then sought relief in the warmer climate of the Florida coast where she remained until her visit to me in April, 1923 During this period the pain, which had from the beginning occurred only spontaneously and without apparent cause, was now initiated by *talking eating*, light drafts of air, or the *slightest touch* upon the right lower lip There have been no paroxysms in the tongue, or in the distribution of the ophthalmic or maxillary branches, and the left side of the face has never been affected

*Examination*—The examination really begins as the patient enters the consulting room If you observe closely and listen attentively to the description of the pain valuable diagnostic data will be accumulated You will notice that she is slightly undernourished, and is much younger in appearance than her actual age Her facies and deportment at the instant give no indication of pain, nor are there any of the ear marks of the "nervous" patient This is strikingly different from the neurotic individual, or the patient suffering from one of the minor painful affections dependent upon pressure or secondary inflammatory disease of the nerve trunk Here, there may be local swelling or redness of the affected part and very often, as the patient enters the room, tonic contractions of the facial muscles is apparent, or the entire hand is held firmly over the painful area In other instances there may be no evidences of pain, but even before the customary greetings are exchanged, the patient speaks of her intense suffering and appeals for immediate relief

In obtaining the history much is to be learned from the manner in which the patient describes the symptoms In this case you will note that, when she is questioned during a quiescent period, the description of the attack is never wanting in accuracy In fact, from her account, or from that of any intelligent patient suffering from major neuralgia, the course of the affected nerve might be sketched upon the face Almost invariably the pain is said to have begun like an electric shock and apparently centered about a tooth, but not in it. These characteristics have already

been noted in the patient's history, and Patrick states that the lightning-like suddenness of the paroxysm has been described by some of his patients as "zip" and "bing" As in this case, the information is often volunteered that the attacks are initiated by talking, eating, drinking, a sudden jar, or light touch upon the skin of the affected part For these reasons, speech is often confined to a movement of the lips alone, or inhibited entirely so that communications are made altogether in writing

These features further serve to distinguish the major type from other neuralgia-like affections of the face The neurotic individual will almost certainly describe, in the minutest detail and with much exaggeration, pain of an excruciating character in an effort to impress upon the physician the intolerable suffering, but, while relating the story, will frequently smile or, in a moment of digression, forget the original cause of the visit Very often the account of the pain is inaccurate, ill-defined, or not definitely localized, and the deportment and countenance are rarely indicative of the imagined distress

Not infrequently the opportunity is afforded to observe one or more attacks during the history-taking and examination and this patient while talking freely suddenly stops, grasps the lower jaw firmly in her hand, closes her eyes, and holds the entire face in tonic contraction After fifteen seconds the attack ceases, the face is again placid, and conversation is resumed by announcing "It's all gone" In severe attacks I have seen a patient beat his head against the wall, or rub the face vigorously with a pad he always carried for that purpose Sometimes chewing movements are made, and the entire face and both upper extremities are in what appears to be voluntary tonic spasm Occasionally the paroxysm is accompanied by edema of the lip or vasomotor flushing of the skin innervated by the affected branch

**Manner of Indicating Pain**—This, without doubt, is a most important and truly diagnostic sign After obtaining the *complaint* my next request is invariably "Take your hand and show me where you have pain" Without exception, the patient *points* to the seat of pain with the tips of the fingers, or more often only one finger, and then outlines the course of the affected branch,

but rarely actually touches the skin This is distinctive, and I have never seen it fail in more than 500 cases The method is, no doubt, resorted to because of fear of inducing an attack by touching the face and the ability to exactly localize the seat of pain When all three branches are involved the same procedure is adopted if the patient is asked to indicate where the attack begins, or to demonstrate the original location of the pain before it had involved the entire trigeminal area

**Physical Examination**—The customary physical examination contributes nothing of a positive character to the diagnostic data Nevertheless, a thorough study of the patient must be made, and this should include a physical and neurological examination, the usual laboratory investigation, roentgenogram of the head and sinuses, and a consultation with the dentist, the oculist, and the otorhinolaryngologist With the exception of arteriosclerosis and hyperarterial tension, examination of this character has not, in my experience revealed the slightest abnormality which might be considered as a cause of the affection Many of my patients have brought with them reports of competent studies in these several domains, and it is noteworthy that these records contain only four instances in which the neuralgia has been associated with any other disorder Cirrhosis of the liver, chronic nephritis, diabetes, and myocarditis were noted respectively in the 4 patients, but I have no record of an instance in which syphilis has been coexistent with the affection The neurological examination reveals no evidence of organic disease of the nervous system, and in this patient the tendon reflexes are slightly but equally exaggerated on the two sides, and the skin of the affected area is hypersensitive to light touch The area of cardiac dulness is slightly enlarged, the retinal and palpable arteries are sclerotic and somewhat tortuous, and the systolic blood pressure is 210 In other respects, the examination discloses no abnormality

## SUMMARY AND DISCUSSION

Major trigeminal neuralgia, tic douloureux, or Fothergill's disease is, indeed, a subjective, symptomatic entity in which the

diagnosis rests entirely upon the clinical history, the character of the attacks, and the complete failure to demonstrate, by the most searching examination, any local or general disorder which can be attributed as the cause of the affection

This single case presented for your consideration is characteristic If you can visualize the patient before you in the amphitheater you have seen not only one case of this disease, but many of them, they all are of the same nature, and differ only in the location of the pain and in individual characteristics

The diagnostic features exhibited in this patient and summarized from my article in "Tice's Practice of Medicine," 1920, are the following (1) The onset of the affection is very rare before the age of thirty (2) With the exception of slight malnutrition due to the inability to eat, the patient has the appearance of general good health (3) The pain *must* be of *short duration,* it must follow the anatomical distribution of the affected nerve, and it must be of sudden onset, paroxysmal, sharp, shooting and lightning-like in character (4) The attack ceases as suddenly as it begins, and is followed by an interval in which there is complete freedom from all pain (5) During some stage of the disease the attacks are initiated by certain forms of peripheral irritation although this may not be demonstrable at all times (6) The *manner* in which the patient *indicates* the seat of pain is distinctive (7) There must be no diminution or loss of any of the cutaneous sense qualities in the trigeminal field

Few physicians escape the patient with some form of face or head pain, but many of us have yet to meet the affection in its major form It is, therefore, equally important that one should recognize certain characteristics of these so-called "minor neuralgias" which at once distinguish them from the type described by Fothergill Thus (1) any pain in the face which begins as a dull ache, increasing in intensity and gradually subsiding, even though accompanied by paroxysmal attacks of a neuralgic character is *not* true major neuralgia (2) Any pain in the face of more than two minutes' duration is, as a rule, not of the major type, but one must be careful in estimating the

duration of the attack I recall an instance in which a patient told me his pain sometimes lasted an hour On one occasion I observed him for this length of time and found that during the period he had forty-two distinct paroxysms with brief intervals of perfect freedom (3) If there is any doubt in the patient's mind as to the location of the pain, or (assuming your knowledge of anatomy to be accurate) if the location of the pain is so ill-defined that you are unable to determine the branch or branches affected, the chances are it is not genuine tic douloureux (4) If, during a paroxysm, the patient can assume an indifferent attitude toward the affection or if the attacks can be aborted by any mental digression it is certainly not major trigeminal neuralgia, and finally, (5) pain in the face associated with involvement of other cranial nerves, loss or diminution of cutaneous sensibility, or other objective evidence of organic disease of the nervous system is not of the major type

**Further Clinical Peculiarities of the Affection** —The disease is slightly more common in the female, and the right side of the face is more frequently involved Because of the marked preponderance of the right sided affection in my series of cases and the wider experience afforded thereby, I never feel quite the same degree of confidence in treating neuralgia of the left side as I do when the right side is involved

The age of onset is usually in the so-called "degenerative period of life", that is from the fourth to the fifth decade Unauthentic cases have been recorded at the age of seventeen, and Patrick obtained histories in two of his patients of an onset at seven and eight, but, as a rule, a history of its occurrence before thirty should be regarded with suspicion The earliest onset in my series is at the age of twenty six

There is no special racial predilection, but the affection appears to be particularly uncommon in the negro, and in my experience at the Johns Hopkins Hospital Dispensary I have met with only two instances in this race

Heredity appears not to play a part in the etiology of the disorder I have treated the affection in a mother and her son, but have no other record in which a family history of the disease

was obtained Patrick found one patient whose mother was said to have suffered likewise, and 7 additional cases in which a distant kinsman was thought to have been similarly affected

The relative frequence with which the three trigeminal branches are involved is interesting, but of little if any etiologic significance The maxillary and mandibular branches are implicated with about equal frequency, but pain which has always been confined to the ophthalmic nerve is rarely, if ever, true major neuralgia I recall the history of a patient who complained of pain only in this branch, and upon his repeated solicitation I was, contrary to my own decision, persuaded to inject the nerve The pain was not relieved A continued search, including eight dental films of a suspected tooth, finally revealed an apical abscess The tooth was extracted and the pain entirely disappeared It is true, that sometimes this branch alone appears to be the seat of a major neuralgic attack, but close inquiry usually elicits a history of pain, at an earlier date, in one of the other trigeminal branches It may have been of only a few months' duration, when it ceased entirely for even a number of years, so that, unless carefully questioned, the patient fails to relate the earlier onset of the disorder Occasionally the attacks are confined to the lingual nerve, and I have seen them involve only the buccal branch of the mandibular division This nerve, you will recall, is purely sensory and innervates the mucous membrane of the cheek When indicating the seat of pain in this region the patient directs the finger along the face from the angle of the mouth toward the tragus of the ear The area thus lies in the overlapping fields of the second and third trigeminal divisions, and one might experience some difficulty, as I once did, in deciding which of the two principal branches is involved The pain, however, is said to be *in the cheek*, it does not radiate to the peripheral field of either the infraorbital or mental nerve terminals, and it is usually initiated by rubbing the tongue against the buccal mucous membrane

**Etiology**—The etiology of major trigeminal neuralgia is not known, and a discussion of the various theories which have been advanced would be of little real value There is much, however,

to support the opinion that the disease is due to a local vascular sclerosis in which arterial spasm probably acts as the inciting cause of the paroxysm Anstie, during the time of Fothergill, expressed a similar idea in the statement that "neuralgia is the cry of the nerve for blood" Vascular sclerosis and hyperarterial tension are commonly associated with the neuralgic patient, and dilatation of the capillaries or local edema are sometimes observed in the domain of the affected nerve following a severe paroxysm These changes, it has been suggested, are consequent upon and not the cause of the affection I have once seen the neuralgia associated with Reynaud's disease and in another instance alternating with attacks of angioneurotic edema It is significant, also, that tic douloureux and causalgia exhibit some striking similarities, and that the vasodilators are the only drugs which seem to possess even temporary therapeutic value in the treatment of neuralgia

**Pathology.**—The pathology of the affection also remains obscure Histologic examination of many gasserian ganglia, by myself and others, have shown really no lesion to which the affection might be attributed, but in my study of the mandibular and maxillary nerves, the accompanying artery was frequently found to be markedly sclerotic with, in some instances, almost complete occlusion of the lumen Recently, one of my surgical colleagues has expressed the opinion that the lesion is of a vascular nature and implicates especially the arteriole accompanying the root of the gasserian ganglion, but in my sections the arterial changes in the root and in the ganglion itself were never so marked as in the nerve branches It is, furthermore, difficult to explain why, if the lesion is situated central to the gasserian ganglion, the paroxysms should be relieved, even temporarily, by any surgical procedure in which the nerve impulse is interrupted peripheral to the ganglion or its root

**Treatment.**—The use of drugs, electricity or the various dietetic, gastro-intestinal, and hydrotherapeutic procedures are without any real or lasting therapeutic value For a time, repeated purgation by the so-called "castor-oil cure," or the administration of gradually increasing doses of strychnine sulphate

had their advocates, but the relief was of short duration and these too soon fell into disrepute In recent years inhalation of trichlorethylene, by placing a few drops of the drug upon the handkerchief and repeating the inhalation at frequent intervals, has been hopefully recommended and employed with variable degrees of temporary relief Only within the past few weeks, I have treated a patient who had used the preparation faithfully for several months and, although the intensity of the suffering was diminished, the attacks were said to have never been entirely relieved I have had no personal experience with any of these methods, but have many histories of patients who have resorted to every conceivable form of therapy other than surgical In one instance a patient brought with him eight typewritten pages of the various therapeutic measures which had been adopted, including thirty-seven attempts to inject the nerve with alcohol I injected the mandibular nerve with alcohol in May, 1928, and he writes, November 25, 1932, that there has been no recurrence

Major trigeminal neuralgia is essentially a disease in which some form of surgical procedure, directed toward interruption of the nerve impulse, must be adopted, and treatment, accordingly, resolves itself into a choice of the several measures which are now in use These are Neurectomy, ganglionectomy, avulsion of the root, fractional section of the root fibers (which has the advantage of preserving when desirable the ophthalmic branch, and thus diminishes the likelihood of corneal ulceration), and finally, the deep injection of alcohol into the maxillary and mandibular nerves as they leave the cranial foramina, or into the gasserian ganglion itself It is this method that I have used since 1910 with satisfactory and unfailing success in relieving the attacks In only two instances, in my earlier experience, have I failed to make a successful injection at the first attempt

The method has, however, met with much adverse criticism, and failed to secure what I am certain is its proper regard It is maintained that the injection gives only temporary relief for a period of about nine months, or that it often fails completely This has not been my experience

The alcohol *must* be injected *into* the nerve trunk or ganglion if the desired result is to be obtained If the injection is made *about* the nerve, the pain ceases for only a few days or weeks, but, more often the attacks continue with increased frequency and intensity I have repeatedly had patients referred to me following these unsuccessful attempts with the remark that the injection method is a failure Injection of the maxillary nerve is sometimes difficult to accomplish with lasting satisfaction There is a small percentage of skulls in which anatomical abnormalities render it impossible to make an entirely successful injection at the foramen rotundum, and it is in the injection of this branch under these conditions that I have obtained the shorter periods of relief When the foramen is accessible, and it is in most instances, the injection is entirely effective, and I have a number of instances in which pain confined to this branch has been relieved for as long as seven to nine years Some of my patients have, I am aware, finally resorted to the major cranial operation, but these are few and so far as I know, only those in whom deep injection of the nerve rather than of the ganglion had been practiced Injection of the mandibular nerve is, as a rule, the most durable of the nerve injections, and when this branch alone is involved relief, varying from five to ten years, might be confidently assured

Injection of the ganglion is quite a different matter, and its choice depends upon the number of branches affected When all three are involved or, in a certain type of skull, even though the third branch alone is affected, effort should be made to reach the ganglion itself In about 8 per cent of the five hundred skulls I have studied in the laboratories in Baltimore, Philadelphia, and Washington it is anatomically impossible to introduce the needle into the foramen ovale, and one must then be satisfied with a deep injection of the mandibular nerve or else resort to the intracranial operation So far as I am able to learn, none of my patients in whom the ganglion was injected have had a recurrence and the earliest case of this type, which I have had the opportunity to follow, was relieved for a period of eighteen years in 1928, since this date my letters of inquiry have not been answered

The patient, who is the subject of this communication, was selected because she has been good enough to send me yearly reports of her condition, and a letter from her, on November 26, 1932, states that she is still free of pain Thus, relief has been secured for more than nine years after injection of the gasserian ganglion, and the resulting anesthesia throughout the trigeminal field is said to persist at the present writing

Since a number of letters to former patients have been returned or unanswered, it has been impossible to secure the desired information in all of my cases, and many of these, treated in the Johns Hopkins Hospital Dispensary, have not been heard of since the original injection In my experience, however, the pain can always be relieved by this method at a single treatment, and upon its return the injection can usually be repeated with equally satisfactory results, but there are a few instances in which, after a time, subsequent injections appear to be less effective

Finally, it has been stated that the injection method is not without danger, that complicating paralyses of other cranial nerves have resulted from its use, or that it might prove fatal if the alcohol is injected into the subdural space It is dangerous, it is a failure, and unpleasant complications are likely in the hands of those whose anatomical training and inability to "feel" through the needle, unfit them to make the injection In conversation with my friend, Dr Wilfred Harris in London, than whom there is no one more skilled in this technic, I learned also that this knowledge of anatomy and this sense of "touch" conveyed through the needle are the essential perquisites of a successful injection

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CLINIC OF DR ERNEST S CROSS

BALTIMORE

## THE SIGNIFICANCE OF EPILEPTIFORM SEIZURES ORIGINATING IN ADULT LIFE

An epileptiform seizure is a dramatic and distressing event at any time of life but when one appears for the first time in an adult who has previously seemed to be in good health, it assumes to the patient and his family the proportions of a tragedy Since major convulsive attacks as well as petit mal seizures do sometimes occur suddenly and unexpectedly in adults, this symptom complex would seem to warrant some special consideration

**Nature of the Epileptic Fit**—From earliest times men have speculated about the nature of epilepsy There is evidence that savage man trephined the skull for this condition Centuries later came the brilliant description of Hippocrates and this has been followed by an ever increasing number of observations down to modern times

Among modern authorities Jackson ascribed the epileptic fit to a violent discharge from a nerve center (psychic, sensory, or motor) due to congestion of blood in the cortical capillaries and retarded movements of blood with altered nutrition of the cells of the cortex Turner believed cerebral anemia to be the cause of the epileptic fit and A E Russell was of the same opinion Fox considered the loss of consciousness and the tonic spasm of the epileptic attack to be due to cerebral vasoconstriction the clonic stage he ascribed to gradual lessening of the vasoconstriction so that some blood reached the brain though not enough to restore normal conditions

Gibson, Goode and Penny made pulse tracings of patients during epileptic fits and studied the blood pressure, they found

no lowering of the blood pressure sufficient, in their opinion, to justify the assumption of cerebral anemia from that cause alone They believed it necessary to look for a local cause in the brain such as local spasm, rather than to general lowering of the blood pressure

Lennox and Cobb have concluded from their researches that there are several conditions of the brain that, singly or combined, may tend to precipitate convulsive seizures First among these they mention insufficient oxygen supply to the cortical tissue Cerebral anemia involving only a small area might depend upon transient spasm of the blood vessels, upon local pressure, or upon some other interruption of the blood supply Investigations in recent years have done away with the old idea of end-arteries in the brain and have shown that the brain cortex is supplied by an endless capillary network anastomosing freely with deeper lying capillaries, the whole cerebral circulation being controlled by the vegetative nervous system, in that stimulation of the vagus nerve causes dilatation of the cerebral vessels, whereas stimulation of the sympathetic causes vasoconstriction

A second state emphasized by Lennox and Cobb is alkalosis due to ingestion of alkali or to hyperpnea It has long been known that forced, hard breathing may be followed by the appearance of tetany

A third state that they mention is edema, in which the tissues are water logged, a thin film of fluid intervening between the nerve cell and its blood (oxygen) supply

Still other states to be considered in this connection are increased permeability of the cerebral tissues to fluid, and increased intracranial pressure

That changes in the cerebral circulation are concerned in the origin of the convulsive process is suggested by the fact that blanching of the cerebral cortex has actually been observed, not only in animals but also in human beings just before the occurrence of a convulsion Nerve cells require adequate oxygen supply for the maintenance of normal function and this supply may be interfered with (*a*) by central sympathetic stimulation as an accompaniment of emotion, (*b*) by local vasospasm,

(*c*) by sclerosis of the arterioles, or (*d*) by edema as in the wet brain of alcoholism, in uremia, and in other general or local conditions that cause edema of the brain

It has been suggested by Foster Kennedy that a sudden alteration in cortical circulation results in a loss of cortical control so that the ungoverned impulses from the lower neurons pour into the muscles and produce the tonic phase of the epileptic attack As the circulation begins to improve, the cortex reassumes control, at first irregularly, in the clonic phase of the fit, and more completely with the cessation of the fit

There would seem to be no good reason to suppose that there is any essential difference between the initiation of the fit of so-called "idiopathic" epilepsy and that of the "symptomatic" variety In "symptomatic" epilepsy, definite gross cerebral abnormalities are present, whereas in the so-called "idiopathic" type of epilepsy, the findings have often been indefinite and hard to evaluate The incidence of "idiopathic" epilepsy is growing less, and we may confidently expect its further diminution as we learn more of the results of prenatal changes, of tiny birth traumata, and of postnatal infections and injuries It is helpful to think of the threshold of neural explosion as a fluctuating one, easily affected by various abnormal conditions, like infections, arteriosclerosis, tumors, or scars To cite Kennedy, "The many types of epileptic expression may be associated with appropriate neural areas which have been the objective of vascular attack, for example petit mal is almost certainly an alteration of consciousness from frontal disorder and the great fit, as has been pointed out, is a sudden, momentary decerebration with a cutting out of the cortical totality followed by a reviving paroxysm of the motor area"

There are many who think that only clonic convulsions are of cortical genesis, the tonic convulsions originating in subcortical regions Personally I do not feel that this matter has yet been fully determined The relations of epilepsy to metabolic and especially to endocrine disturbances have been much discussed but it is as yet too early to speak decisively about such relationships

**Incidence of Idiopathic and Symptomatic Types**—Idiopathic epilepsy, as is well known, makes its appearance in a large percentage of cases in childhood or during adolescence, though rarely it may appear later On 6595 cases reported from the Craig Colony at Sonyea, New York, 83 5 per cent had onset of convulsions within the first thirty years of life Gowers found 89 5 per cent of 3002 cases had initial convulsions within the first twenty-nine years of life Among the "idiopathic" cases are to be included the inherited type (recessive mendelian inheritance) and the type due to germinal injury in the offspring of drunkards and syphilitics

In general, epileptiform attacks of late development are symptomatic of some definite underlying pathologic condition It is my purpose in this clinic to describe some cases of symptomatic epilepsy and to emphasize certain important points in diagnosis and in management In my experience, the commoner causes of symptomatic epilepsy are syphilis of the nervous system (including general paresis), chronic alcoholism, lead poisoning, brain tumor, and cerebral arteriosclerosis, other less common causes are encephalitis, meningitis, multiple sclerosis, and sequelae of traumata to the head

## ILLUSTRATIVE CASES OF SYMPTOMATIC EPILEPSY

**Case I**—Miss N D C , twenty-nine years old, was referred in October, 1928, by her home physician for the investigation of her recurring convulsions The first attack had occurred about a year previous to consultation, having its onset a few hours after a party at which a considerable amount of alcohol had been consumed The patient reported that she awoke with rapid pulse, jerking of the right leg and throbbing in the right side of the abdomen, and that these symptoms were soon followed by unconsciousness that lasted for a few minutes In all there were about six convulsions in the course of the year and the manifestations in all of them were quite similar The attacks were preceded by a warning which she described as a "flash" in the epigastrium There was, she said, a sense of something impending, then the right leg would begin to twitch, followed by loss

of consciousness If the patient had time to put her handkerchief into her mouth she could prevent tongue biting but she was not always able to do it During the period of unconsciousness her friends observed general convulsive movements affecting both sides of the body After each attack the patient felt weak and stupid and she would remain in bed for the rest of the day suffering from headache On one occasion at least there was urinary incontinence The latest attack had occurred three weeks before the consultation

On inquiry, it became evident that the patient had been living under great nervous strain for several months at least in connection with her work in caring for juvenile delinquents She had used alcohol rather too freely, and up to the time of the first convulsion she had been drinking some ten or twelve cups of coffee each day A study of the family history revealed several interesting facts The father and mother of the patient had been divorced The father was a heavy drinker One sister was said to have dementia praecox

On physical examination, the patient was found to be 14 pounds below calculated ideal weight There were several suspected teeth, the pulse rate was 100 per minute

Blood, gastric juice, and stool showed no abnormalities The blood Wassermann reaction was negative. The urine showed a trace of sugar but the fasting blood sugar was only 90 mg per cent The pelvic examination was normal, and the basal metabolic rate was also normal

On x ray examination, one devitalized tooth showed a definite periapical involvement

Detailed neurological examination failed to show any evidence of organic disease of the nervous system The eyegrounds were normal, but the ophthalmologist reported some contraction of the fields of vision and a moderate refraction error Ventriculography showed a filling defect in the posterior part of the body of the left lateral ventricle with a calcified area lying just over the defect

A diagnosis of tumor of the left cerebral hemisphere was accordingly made and cranial operation was advised. A little

delay ensued while the patient was making up her mind about operation Approximately four months later, however, the patient returned to Baltimore and operation disclosed a glioma on the left side of the brain in the postrolandic area The tumor lay deep and had invaded the motor tract to some extent, but it was finally removed completely and the patient made a satisfactory recovery

Case II —Mr K I L , sixty-five years old, referred for diagnostic study by his physician in November, 1929 About one year before the consultation a convulsion had occurred in the middle of the night and had lasted for ten minutes There was tongue biting but no sphincter relaxation Three months before the consultation another convulsion had occurred, also in the night For several months there had been occasional little "spells," during which the patient would be dazed for a minute and complain of dizziness He was reported to be forgetful, irritable and to show easy fatigue Six years earlier there had been a period of several months during which the patient occasionally became dizzy and dazed for a few minutes but without loss of consciousness Under treatment, including the use of luminal, these symptoms had been relieved The patient's father, who died at fifty-two, had developed epilepsy at the age of thirty-three and toward the end of his life had had two or three attacks daily

On physical examination, the findings were negative except that the patient was 25 pounds under calculated ideal weight, the temporal arteries were tortuous and the blood pressure was 145 systolic, and 80 diastolic

The blood Wassermann examination was negative and the blood count was normal There was complete achylia gastrica The urine showed several hyaline and one finely granular cast with a minimal trace of albumin

Neurological examination was negative except for slight general exaggeration of the deep reflexes with some special accentuation of the left knee jerk The eyegrounds showed no pathologic changes On account of the dizziness the condition

of the vestibular nerves was investigated but no abnormality could be demonstrated The spinal fluid was reported negative by the physician who brought him and this test was not repeated Ventriculography yielded negative findings

*Diagnosis* —Epilepsia tarda, probably dependent upon early cerebral arteriosclerosis

Case III —Mr S V I, forty three years old The patient was referred for diagnostic study in October, 1922, because of an illness that had begun in the preceding January with a convulsion that persisted for half an hour Two weeks before the consultation he had suffered another convulsive attack in which he smelt a very disagreeable odor which he referred to his nose, during the unconsciousness that followed his face turned black according to the report made by his wife The perception of bad odors in the week or two before consultation was thought possibly to be the result of sinus infection but no such disease had been demonstrated

The patient admitted that four years previously the blood Wassermann examination had been reported strongly positive, treatment had been desultory because of the patient s fear that someone would find out the actual nature of his trouble At the time of the first convulsion, the spinal fluid was reported to have shown a four plus Wassermann reaction, following which intraspinal treatments were instituted

The family history was unimportant except that the Wassermann reaction in the wife's blood was reported strongly positive four years previously and specific treatment had been instituted

On examination of the patient the positive findings included deafness, pyorrhea alveolaris, a nodular thyroid, and undernutrition There was no evidence of peripheral arteriosclerosis and the blood pressure was 120 systolic, and 75 diastolic.

The blood count, gastric juice, stool, and urine were negative The blood Wassermann reaction was positive, the cerebrospinal fluid showed a positive Wassermann reaction, positive globulin and a cell count of 55

Neurological examination showed sluggish pupils, some incoordination of the lower extremities, sluggish knee jerks and absent ankle jerks, with considerable swaying on walking along a line The memory was defective and the speech was somewhat hesitant There were mistakes in calculation, slight slurring of the speech and a little overactivity of the muscles around the mouth during speech The ophthalmologist reported the fundi to be a little redder than normal but there was no other fundal lesion

The patient was kept under observation for a month, during which vigorous antiluetic treatment was instituted The spinal fluid Wassermann remained positive, however, and the fluid showed a paretic curve

A diagnosis was made of taboparesis, though it was evident that the brain had suffered considerably more injury than the spinal cord so that the paretic symptoms were more prominent than the tabetic

Case IV —Mr S N U , aged fifty-five, was seen in consultation in 1927 because of an illness characterized by two epileptiform attacks in the preceding twenty-four hours, one attack one month previously and three attacks ten years previously The patient had amnesia for each of his attacks and for most of the events of each preceding day His calculation was markedly disturbed and he was disoriented as to time but not as to place or person He had had definite hallucinations the night before, he said that he had seen red dogs and children in his room Fever to 101 F had been present No reliable history could be obtained from the patient but it was ascertained that he had been addicted to the use of morphine for many years, having begun its use on account of chronic trouble with infected varicose veins No other important factors in the case were available at that time

Examinations revealed undernutrition (approximately 20 pounds), suspect teeth, diffuse bronchitis with râles throughout both lungs, auricular fibrillation with pulse rate about 134, and old varicose vein scars There was some leukocytosis Within

twenty four hours the temperature became normal and the mental state much clearer At the end of forty eight hours the white blood count had become normal and under digitalis medication the fibrillation had disappeared The pupils were active and equal the left eyeground was negative but because of immature lens turbidity the right eyeground could not be seen The reflexes showed no abnormalities

*x* Ray examination of the skull revealed a normal sella turcica There was no evidence of increased intracranial pressure The paranasal sinuses were clear, *x* rays of the teeth showed no evidence of infection The heart was not increased in size but was of the pendulous type with normal, regular pulsations Examination of the cerebrospinal fluid showed the presence of six cells and a negative Wassermann reaction The blood Wassermann was also negative

The patient then improved rapidly, gaining weight and showing no further fibrillation, fever or convulsions Lues was ruled out Brain tumor was considered most improbable but a definite conclusion as to the origin of the convulsions could not be reached at the time

In September, 1927, the patient had a series of five or six convulsions At this time it was possible to establish the fact that preceding the series of convulsions the patient had been alcoholic, taking as much as 26 ounces of gin in one day, and the admission was made that alcoholic excesses had preceded each one of the previous illnesses that were characterized by convulsions During the winter of 1928 and 1929 there was again excessive use of alcohol with resulting petechial eruption of the skin of the lower half of the body, dyspnea, auricular fibrillation, nausea, and vomiting

In May, 1930, another series of convulsions occurred during which there were ten or more epileptiform seizures terminating in a stuporous condition of several days' duration The patient denied that alcoholism preceded this episode and no definite light could be thrown upon that phase of the situation, though it was certain that 7 or 8 grains of morphine were being taken daily

A few months later the morphine addiction was successfully treated by gradual withdrawal At that time the blood Wassermann was again reported negative and no increase in blood bromide was demonstrated This examination was carried out because the patient had taken luminal and bromide steadily since the convulsions of 1927 A report from the patient's physician one year later indicated no return to morphine and no recurrence of convulsions but there was again an alcoholic tendency It seems probable that alcoholic excesses, with wet brain, were the precipitating causes of these recurring series of convulsions

## DISCUSSION OF THE FOUR CASES

Case I —Presented several interesting features The age, twenty-nine years, was above that at which so-called "idiopathic" epilepsy usually develops, and yet up to the time of the ventriculographical report no organic basis had become evident The alcoholic indulgence had been comparatively mild and did not seem sufficient cause for the symptoms The family history suggested the possibility of a neuropathic constitution in which might reside the so-called "epileptic" tendency The hemoglobin and red cell count were within normal limits and no stipple cells (the earliest and most constant finding in lead poisoning) were found on careful examination of stained blood cells, which turned us away from the idea of lead poisoning As to the possibility of lues, the blood Wassermann reaction was negative, but examination of the spinal fluid was deferred in view of the fact that ventriculography seemed to be indicated, despite the fact that the more characteristic signs of brain tumor were lacking, thus, headache had been rare, the eyegrounds were normal (as reported by three different examiners), vomiting had occurred only three or four times in the year, and dizziness was reported only after the convulsions Furthermore, examinations of the cranial nerves, the motor and sensory nervous systems and the reflexes, had revealed no deviation from the normal The patient, however, was sure that in each attack twitching of the right leg had occurred before loss of consciousness and before the

general convulsive movements That this was a significant observation was proved by the fact that at operation a glioma was found in the left postrolandic area undermining the ro landic vein and invading the motor tract with a projection that must have extended so as to be close to the internal capsule

That brain tumor is frequently accompanied by epileptiform attacks is clearly shown by the figures of Parker, of the Mayo Clinic In 313 cases of brain tumor coming to necropsy, grand mal had been present in 67 or 21 6 per cent Syncope, stupor, petit mal, tonic spasms in jacksonian attacks with retardation of consciousness were excluded from his figures He showed that the tumors accompanied by convulsions are practically al ways situated above the tentorium Such tumors are usually found in the frontal, parietal, and temporal lobes of the brain, convulsions are excessively rare in connection with tumors of the cerebellum, the cerebellopontile angle, fourth ventricle, the pons and the medulla It is interesting, in passing, to observe that increased intracranial pressure alone cannot be the cause of convulsions because such pressure is prone to be highest in tumors situated below the tentorium and these tumors as we have just seen are very rarely accompanied by convulsions

Case II —Is interesting largely because of the paucity of the findings Perhaps the epilepsy should be considered as having been dependent upon an early arteriosclerosis though the retinal vessels showed but little evidence of sclerotic change. Forgetfulness, irritability, dizziness, easy fatigability, and convulsions in a patient of fifty five suggest the possibility of arterial degeneration, and we know that the distribution of cerebral ar teriosclerosis is notoriously variable and capricious Perhaps this man's threshold of neural explosion may have been low in view of his father's epileptic tendency and so easily set off by comparatively mild alteration in the cerebral circulation

Case III —Presented relatively little difficulty as a diagnostic problem because the infection with syphilis was admitted, mental changes were marked, and evidences of a spinal cord

lesion were discoverable on physical examination Persons exhibiting predominantly tabetic changes do not often suffer from epileptiform seizures, but both grand mal and petit mal attacks are fairly frequent in general paresis and in the interstitial type of cerebral lues The latter type may symptomatically strongly resemble brain tumor in the presence of headaches, optic neuritis, and vomiting

Case IV —Emphasizes the importance of a complete history The attendants of this patient had not realized the significance of the alcoholism and had unwittingly concealed the fact of its existence at the time of the first consultation

## DIAGNOSIS OF THE CAUSE OF SYMPTOMATIC EPILEPSY

It is evident that the investigations made must, in many cases, be exhaustive if we are to feel satisfied with our diagnostic efforts to elucidate the causes of epileptiform attacks The history must, in the first place, be carefully scanned for any possible suggestive points On physical examination, particular attention should be paid to the vascular system for evidences of degenerative disease, and to the nervous system for suggestions of earlier infections, irritations, or pressure When we have to deal with either syphilis or brain tumor it is obvious that early diagnosis is of very great value and so we should promptly resort, in cases that are suspect, to examination of the spinal fluid, on the one hand, and to ventriculography, on the other The latter procedure should not be attempted, however, except by an experienced operator

After the cases due to syphilis, to brain tumor, to lead poisoning, to uremia, to alcoholism, and to gross arterial change have been culled out of the group of late-developing epileptiform seizures, there will still remain a number of cases in which no marked cerebral disease can be proved to exist Some of these may depend upon small, slow-growing brain tumors which may be revealed only after a longer period Such cases require, of course, careful watching and neurological examinations at regular

intervals Finally in this residual group there will be certain patients who, under appropriate treatment may indefinitely continue their usual occupations with but little interruption It is to be emphasized that there is a fairly large number of such relatively favorable cases, knowledge of the existence of these may be a great comfort, both to patients and to physicians

### TREATMENT OF SYMPTOMATIC EPILEPSY

The nature of the treatment is of course obvious when a removable cause can be discovered In the other cases, phenobarbital in doses of from 1 to 3 grains in the twenty four hours may be of the greatest help in the prevention of attacks the sedative effect of the drug evidently raising the threshold of neural explosion

It is often possible to get along successfully with relatively small doses of phenobarbital A very good way to proceed is to give $\frac{1}{6}$ grain five times daily and gradually increase to $1\frac{1}{2}$ grains three times a day, after a dosage has been reached at which the attacks no longer occur, one may gradually decrease the dosage until the minimal effective amount is determined

If the older method of treatment with sodium bromide should be tried, the amount of common salt in the food should be reduced, the bromide content of the blood should be estimated occasionally in order that bromide intoxication may be avoided

In status epilepticus, the bowel should be emptied and venesection done The heart should be supported by digitalis and by camphor preparations if necessary In very severe cases an anesthetic may be administered

In addition one must review all the somatic and psychic elements involved in each case and attempt to eliminate as far as possible any suspected precipitating factors of the attacks It should be explained to every epileptic that because of our inability to be sure just when an attack may occur, he is a potential source of danger, both to himself and to others Certain occupations are, therefore, obviously unsuitable for epileptics.

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# CLINIC OF DR LESLIE B HOHMAN

HENRY PHIPPS PSYCHIATRIC CLINIC JOHNS HOPKINS HOSPITAL

## PRESENTATION OF A CASE OF HYPOCHONDRIACAL DEPRESSION

THE first patient I want to present to you is a married man of thirty nine years of age who consults us because of "abdominal distention, particularly after meals," and constipation These gastro intestinal symptoms are accompanied by a feeling of being "washed out physically and mentally" Although the patient sleeps well, he gets up in the morning feeling more tired than when he goes to bed at night He finds that carrying on his job is very difficult, because he is trying to avoid people and finds that addressing groups of employees, although it is a necessary part of his job, is intolerable He develops a very real anticipatory fear when he knows he is going to be forced to talk to anyone The patient has been sick for about eight months and during that period has lost 20 pounds in weight and fears that this may be due to thyroid disease When we examine this patient physically we find that nothing strikingly abnormal can be made out, except some slight abdominal distention The patient is concerned because his collar feels so tight and he is fearful that his thyroid gland is enlarged Examination fails to reveal any thyroid swelling

This is not the first time the patient has been sick with symptoms such as he has at present In 1928 he went through a similar attack which lasted for several months and at that time the symptoms were exactly the same as they have been in this attack. A very thorough study was made then and the following positive facts were recorded—a somewhat enlarged thyroid was found and a somewhat distended abdomen His basal

metabolism rate was −12 An x-ray of the gastro-intestinal tract showed a markedly spastic colon, and a long segmented appendix Visualization of the gallbladder, by intravenous dye, revealed a normally filling and emptying gallbladder The test meal revealed an achlorhydria

His former physician made a diagnosis of "vagotonic spastic enteritis" He was given doses of thyroid extract, hydrochloric acid, and belladonna He improved over the next few months and finally dropped all medication He remained well until eight months ago

Now what does the psychiatric examination of this man reveal? Let us first examine the fact of his life surrounding the period just before both of his illnesses Preceding the first illness he had been employed for twelve years by one concern and had worked himself up from the job of office boy to that of vice-president in a large mercantile establishment He was quite happy in his work but each year when it came to the time for his firm to pay his yearly extra bonus, they failed to fulfil their promises of the preceding year This irked and irritated the patient, and although he always got his bonus finally, the last time the situation arose the patient resigned in a temper This was in the period of financial expansion and the patient felt independent and safe Although he was well regarded in his industry, and found another job fairly promptly, he had to take a job with a somewhat smaller business and the adjustments in business method that this required were difficult for him He realized that he had made a mistake to leave a concern in which the business methods were thoroughly congenial to his taste, because he found himself involved in high pressure, driving, somewhat unscrupulous business methods which were the general rule in the industry About this time his first symptoms began He stayed with this job for a year and made a success of the venture and was then offered a better job with a more reputable concern As he achieved success his symptoms gradually became better but throughout the next two years his job became increasingly difficult and the last six months he held it, he knew that even if he did not lose his job the working conditions would

be intolerable. His boss was a driver who was ruthless and completely unpredictable No one in the organization ever knew when he was to be humiliated before the entire organization Due to a retrenchment policy because of the economic depression, the patient lost his job at the end of the two year period Although he was relieved to be quit of this particular boss, he was disturbed that he could not immediately find a job He had exhausted his resources through stock market speculation and without a job, he became more discouraged and depressed When he did finally accept a position it was for less than half of his former salary and with an organization whose methods were unsympathetic to him

The patient had been the most successful member of his family and was the chief support of his parents Although he always felt inferior to his brothers and sisters on the score of education, the fact that he was able to direct the family financially had compensated for his inferiority The patient had delayed marriage until two years ago His responsibilities at a time of decreasing income, increased Although he was able to balance his budget, for the first time in his life he found himself living without a margin of financial safety

Let us make a formal psychiatric examination of this patient His *general attitude and behavior* would give no clue to any abnormality except that he is somewhat sober in his appearance He says that he does not carry himself as well as formerly but this would not be apparent to any observer There is no disturbance in his *stream of talk*, although he is occupied essentially with his complaints, and is willing to talk constantly of his symptoms He shows no slowing in his speech or any difficulty in thinking, but complains of inability to concentrate well He is obviously well *oriented* When questioned about his *mood* he says he "feels depressed and washed out" He says that after a good night's sleep he wakes up feeling very badly Throughout the whole morning he feels so heavy and dull that he can hardly keep his eyes open, and unless he exerted his will to the utmost he would try to avoid all business, and would go home He feels even worse after lunch but from then on he becomes brighter

and by evening he feels fairly well Along with this depression the patient complains that he has no energy or "pep" He has lost all his interest in his business and pleasure In addition to this mood of depression, at times he complains of feeling anxious, with feelings of being suffocated, his heart palpitates and the palms of his hands are "sweaty" and "clammy"

The *content* of the patient's thinking is normal except that he is apt to depreciate himself He thinks that every interview he has in business turns out poorly, although he admits that actually he succeeds in winning any point he has tried to make and brings to successful issue every business transaction which he has attempted He feels that he has been a failure, that he has made poor use of his life, and that he made an irretrievable mistake when he quit his twelve-year job He thinks that the future is dark and that he is too old ever to really establish himself successfully again His *insight* into his state of mind is really excellent When it is pointed out that he is in the same position as everybody else, and that he has an excellent chance to "come back" because of his recognized skill, he admits that he is overpessimistic, but, without constant reassurance he falls back into his gloomy depression Objectively there is no break in his *judgment* although he is constantly doubting his ability to make correct judgments

Here then we have a patient who complains of abdominal symptoms and loss of physical energy, and whose condition is not explained by any adequate physical disability His mental examination reveals the positive facts that he is depressed and fearful, that this depression is accompanied by loss of interest and ambition, and has brought in its wake a lot of self-depreciation His sex function is lowered and his appetite is poor and has resulted in a marked loss in weight We learn that all of his symptoms are worse in the morning than in the evening We learn further that this is his second attack and that the first attack terminated after a period of eight months Both attacks were precipitated by unfavorable business situations

An inquiry into his past life showed us that we were dealing with a man who had put all of his interest into making money

and who had compensated for his lack of education and cultural interests by stressing money success

This type of case represents a very important group of disturbances, which frequently escape correct diagnosis and understanding With incorrect diagnosis adequate treatment and prognostication cannot be given and serious danger to the patient may follow

The diagnosis in cases of this type must rest upon the knowledge that the illness is a variety of emotional disturbance and that the emotional disorder is the primary and most important symptom Emotional disorders of this sort are closely allied to, if not the same as, the manic-depressive psychosis The fact that the patient's conduct does not become sufficiently disturbed or distorted to produce any noticeable abnormality of behavior does not mean that we are not dealing with an essentially mental disorder The course and outcome of (emotional) depressive reactions of this sort are exactly the same as the more disturbed manic-depressive type of case which is so regularly seen in mental hospitals We know that we can predict recovery from the depression and that this recovery will occur at the end of a period of weeks or months, no matter what the conditions in the patient's life are. That is, we are dealing with an illness which will run a limited course and will terminate in recovery When I say that the depression is the important and primary symptom I mean that all the other symptoms which are so disturbing to the patient and for the cure of which the patient consults us, will disappear when the depression disappears As long as depression holds on, the same symptoms or similar ones are apt to dominate the clinical picture

Whenever we are confronted with a case in which the physical findings or history do not provide an adequate organic basis for an understanding of the symptoms or condition, we must immediately think of the possibility of a psychiatric disturbance. The *second question that should concern us is, are we dealing* with the type of case which belongs to the circumscribed variety illustrated by our patient, or are we dealing with a type of neurosis which will not terminate spontaneously at the end of a given

period of time? We might draw an analogy to pulmonary tuberculosis and lobar pneumonia We know that pulmonary tuberculosis will not heal spontaneously, but that recovery is dependent upon the severity of the process and upon proper treatment, *i e*, to say we are not dealing with a self-limited disease

Lobar pneumonia on the other hand does belong to the group of self-limited disease and barring accidents or complications will terminate after a definite number of days Now the patient who presents himself with physical symptoms which are "functional" belongs either to a group analogous to pulmonary tuberculosis—these we call psychoneuroses—or to the group analogous to lobar pneumonia—and these we call "affective" reactions When we say "affective" we mean emotional and that a type of emotional disturbance dominates the person The emotion is usually one of depression but may at times be fear, or anxiety, or elation

Now what does the examination in this case show us of the essential nature of this depressive (affective) reaction The patient complains frankly of depression (it is important to give the patient an opportunity to express his mood frankly without leading questions Questions such as "What is your mood?" or "How are your spirits?" although somewhat stilted are the best types of question) Instead of a frank statement of depression, such as "I feel depressed, or blue, or melancholy" one may get the answer, "I feel disgusted," or "washed out," or "miserable," or "scared," or "anxious" We see further that this mood disturbance shows a very definite diurnal variation That is, it is usually less severe in the evening than in the morning, although the reverse may be true In this particular case there is no disturbance of sleep, but usually the patient's sleep is poor and he frequently wakes early in the morning, especially if any symptoms of anxiety are present The appetite is poor, as with our patient, and a loss of weight frequently follows Whereas our patient shows no slowness in speaking or thinking, this is frequently not the case Patients often find themselves "slowed up" or retarded in both speech and thinking Our

patient shows a definite loss of energy, and interest, and ambition, and furthermore has lost his interest in sex to a large degree It is interesting to note that a loss of sex interest and power is very common in these affective disturbances and not infre quently a patient will consult a urologist for loss of sex power when he is in the midst of a depression

Along with the loss of pep and energy and interest, the pa tient frequently blames himself about many things and feels that he has made mistakes in judgment and in a variety of de cisions The tendency to self-depreciation may go so far that the patient distorts facts to fit his feeling of unworthiness Not infrequently a man may feel that he is ruining his family or bringing disaster to them, etc Indecision becomes a very ac tively disturbing symptom Patients find it difficult to make the simplest decisions without a lot of conflict, and no sooner is a decision made than there is regret that the opposite one was not made One of my patients who consulted me and an internist for "heart trouble (his heart is perfectly normal) has been so indecisive that twice he has let contracts for building a new house and twice cancelled them—the last time excavation had started and the lot had to be refilled He was so indecisive that he could not let the decision stand either way His family finally stepped in and insisted that the house be built Another patient who was referred to me by an internist because the pa tient had severe abdominal pain and was fearful that he had cancer The physical examination revealed no abnormality and ten years of recovery from the abdominal pain has demon strated that the patient was not organically sick He has had subsequent attacks of depression but he is still physically well In his first depression he was so indecisive that he made two trips to Europe and did not get off the boat either time He could not decide to stay at home or remain in Europe

Along with the depression almost any type of physical symp tom may be present. Any organ of the body may be the center of hypochondriacal complaints These complaints may so closely simulate physical disease that the physician can only exclude organic factors by the most careful examination I do

not believe that one is ever justified in regarding any symptom as psychoneurotic until the most careful studies have been completed The fact that a patient is, or has been known to be, neurotic does not exclude the possibility of organic disease One not infrequently sees tragic mistakes in which the patient has been neglected because doctors have made a "snap" diagnosis of neurotic symptoms My impression is that it is not the psychiatrist or neurologist who errs in this direction but the physician who does not establish the invariable rule that in every case there must be careful and complete examination

In this type of affective disorder we find that the memory, both for remote and recent events, is objectively good The patient, due to the slowness of his thinking or talking, may have a subjective difficulty with memory, but objectively no difficulty is discoverable

Now how are we to distinguish these self-limited affective disorders from the psychoneurotic states that are not self-limited? In the first place the onset of the affective (depressive) illness is usually somewhat acute The patient can date the onset of his illness to a fairly definite date The depression usually makes its appearance either at onset or soon after the appearance of symptoms Secondly, the attack is apt to be induced by some unusual environmental strain There is likely to be some specific difficulty which has upset the patient Although it is possible that this type of illness may appear to come "out of the blue," as it were, still this is not the rule Ordinarily one discovers some specific psychologically upsetting situations with which the patient is having to deal Thirdly, many of these affective disorders occur in patients in whom there is a constitutional bias toward depression One frequently discovers a history of "nervous breakdowns" in the family—father, mother, siblings, or collaterals This is not always the case, in fact one not infrequently sees cases in which no history of nervousness in the family can be elicited Fourthly, since this type of illness is frequently a recurrent type of illness, it is important to search carefully the past history of the patient for former attacks I can remember a patient who was saved from an abdominal ex-

ploration by asking the question, "Have you ever had this before?" He had profound obstipation, a mass in the region of the ascending colon, and the *x* ray findings were equivocal The internist in the case was not satisfied with the surgeon's readiness to explore, because he gave due weight to the fact that the patient was very depressed The history of the patient revealed that thirty years before, the same illness had baffled his physicians and had terminated in recovery after a period of months of depression Fifthly, the symptoms of the depression which I have outlined in the mental examination make the positive diagnosis of a circumscribed affective illness not difficult.

You may have noted that I have not mentioned anything about the sex life of our patient, that I have not told you that he was married three years ago and has one child and that his marriage is a happy and satisfactory one I do not seem to suggest by this omission that I do not regard the sex life as one sphere in which much stress and strain may occur, but as only *one* of such spheres In this particular case I do not believe that sex plays an essential rôle I think it very important that the study of the sex life be as thorough as all the other examinations, but not that it be regarded as the only source of psychological difficulty All human relationships and values and situations can become the focus of psychological involvement and it is our job to study each man for his particular difficulties

Now having arrived at a correct diagnosis, what can we do in the way of therapy?

Therapy must be based upon a clear understanding of the nature of these depressive (affective) illnesses One must realize in the first place that although recovery may be expected to occur spontaneously at the end of a period of weeks or months, nevertheless the exact length of the period is unpredictable The physician can only give assurance that the illness will terminate in recovery but any statement as to the exact time is merely guessing Illnesses of this sort usually last from three to six months as the minimum, and may persist for three or four years Shorter and longer illnesses are not rare Since the duration of such an illness is not known, it is difficult to judge whether

therapy of any kind does anything to shorten the course of the attack We must accept the fact that we have no "specific" therapy for the depressive (affective) illness In some cases, however, psychotherapy is distinctly helpful and seems to be able to cut short an illness which we would have reason to suspect might last much longer (if one may judge in part from the length of former attacks and the speed with which the particular attack is cut short after psychotherapy begins) It is in the cases which we call "reactive" depressions that specific psychotherapy is apt to be useful From a study of normal human psychology one would suspect that if one could remove the causes which had started depression one could stop the depression This is true only in a limited number of cases To prove the inability of the patient to have depression dispelled by the correction of this situation which precipitated it, we can quote the case of a man of fifty-eight, who became depressed after the loss of his entire fortune in a law suit against his business partner Six months after the onset of the depression, a superior court reversed the lower-court decision, and the patient had his fortune restored But the depression was not relieved and another nine months intervened before recovery took place

One cannot therefore assume that the correction of even the precipitating psychological factors of an illness will result in recovery On the other hand, one, from time to time, sees cases in which depression and accompanying hypochondriasis are promptly relieved by the elimination of disturbing psychological factors For example, one of my patients has consulted me on three separate occasions over a period of fifteen years complaining of visual scotomata and ringing in the ears Each time he has been depressed for several months before I have seen him I have found each time that he has been involved in some frustraneous sex affair, and has not had the wisdom to see what was causing his difficulties He was brought up in a very rigid, moral, religious background and, although his marriage has been unsatisfactory, he does not wish to dissolve it, but has not the strength and courage to avoid extramarital sex entanglements even though his moral attitude is actively opposed Each time

he can be persuaded to start afresh and honestly his depression and symptoms promptly disappear

I would therefore say that, although one cannot promise active psychotherapy in most cases, still there are cases in which specific psychological situations are etiologically responsible, and in a certain number of these cases recovery can be speeded up by the correction of the disturbing situations

Even, however, if no specific therapy is available there is much to be done for the patient Reassurance is of great advantage to make the course of the illness less severe and painful Patients can almost always be made to feel less depressed and hopeless by daily reassurance of recovery When they are told that recovery is certain and is not dependent upon an effort of will, but will come no matter what happens, the discouragement is greatly relieved Families and physicians in attempting to force the patient to pull himself out of the depression by an effort of will, are apt to increase depression, because the patient feels guilty over his failure to recover—a failure which is inevitable

There is one active danger in all depressive cases and that is the danger of suicide Every depression is potentially suicidal One must, therefore, see to it that in so far as possible the patient is not left alone, particularly during these periods when the depression is deep and the patient seems desperate No one is a good judge of whether a depressed patient is suicidal The old lay notion that when a patient talks about suicide he is safe, is simply not sound The wise physician is always on guard and, if the depression deepens, takes all precaution to have the patient under adequate surveillance at all times I cannot stress too strongly this danger of suicide It is infinitely wiser to err on the side of overcaution

Sleeplessness is a problem which calls for the wise use of sedatives Sedatives in the usual doses can be used with safety—*i e*, without the danger of habit formation The illness is self-limited and therefore when recovery takes place sleep rights itself as does the other symptoms It is frequently helpful to use small doses of barbital or luminal during the daytime—

tension and depression are thus frequently relieved One can use $1\frac{1}{2}$ to $2\frac{1}{2}$ grains of barbital three times a day over long periods of time without deleterious effects We invariably prescribe sedatives in capsule form, so that when improvement becomes evident, cornstarch or bicarbonate of soda can be substituted in the capsules There is undoubtedly a period during convalescence when the suggestion effect of drugs is valuable It helps to maintain the patient's confidence By this method, by the time recovery has taken place, the patient need not be taking any drugs whatever

Loss of weight must be guarded against because appetite is so often poor We frequently insist upon daily weighing in order to convince the patient that an adequate amount of food is not being consumed A regaining of weight is encouraging to the patient and does increase his sense of well-being

Another active therapeutic need is to prevent the fixation of physical symptoms after recovery from the depression Unwise stressing of minor physical abnormalities may convince a patient intellectually that he has some physical disease, and unless the physician recognizes and stresses the essentially functional nature of the symptoms the patient may be left with the conviction that he has some serious organic disease Our first patient had physical disease so stressed that it is not clear to him now that he has not thyroid disease After all when a patient is given thyroid extract after being told that his basal metabolism is somewhat low, he cannot be expected to distinguish between the idea of thyroid disease and laboratory findings Our patient had a basal metabolism rate which was at all times within normal limits (minus 12 and plus 5) I have one patient who, after a year's depression, was so convinced by his physician that he had serious gastro-intestinal disease, that he has lived on a rigid diet for twenty years He could have been spared all of this gastro-intestinal preoccupation if his physician had given him correct information in his original attack

There is another point of therapy that is essentially prophylactic If one studies carefully the psychological and situational stresses and strains which precipitated the illness it is frequently

possible to give the patient a program of mental hygiene that will prevent recurrences for the future Frequently these depressive illnesses occur in persons who are cyclothymic in disposition—i e, they are people who are either "way up" or "way down" in their moods These moods may be of very short duration and normal for the individual, but frequently they are prolonged into serious pathologic depression if the situations involving them are severe One recommends more frequent vacations for the person who has too exclusive an interest in excessively hard work, for others a broadening of interests and the adoption of hobbies and avocations, frequently a marriage situation can be adjusted by the impersonal advice from a physician from time to time Whereas some patients need an increase in interests, other patients need simplification of life Sex problems can be frequently adjusted by the physician by the use of patient understanding and wise advice If the physician has the patience and wisdom to carefully study the problems of the patient's life, he can frequently find methods of easing the stresses and strains and thus can be done without any startling shifts or changes in the patient's life A good common sense attitude can give most gratifying help

To summarize We have presented to you a type of illness in which physical symptoms are as the manifestation of an underlying depressive (affective) illness This illness runs a course and results in recovery Correct diagnosis is made on the basis of constitutional factors, nature and course of the illness (dated onset, depression, diurnal variation in symptoms, slowness in talking and thinking, loss of energy and enthusiasm, reduction in sex interest, self-occupation and self depreciation sleeplessness, loss of appetite and insight) Therapy has been outlined

## CLINIC OF DR NORMAN B COLE

JOHNS HOPKINS HOSPITAL

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## COMMENTS ON A CASE OF POLYCYTHEMIA RUBRA VERA WITH AUTOPSY

POLYCYTHEMIA rubra vera, or erythremia, is still sufficiently rare to warrant the reporting of new cases, and especially of those which offer diagnostic pitfalls The case here presented is held to be one of true primary polycythemia, it is interesting because of a number of features bearing on the differential diagnosis

R C a white male school teacher of thirty three years, was first seen on January 21, 1932 in the clinic of Dr Lewellys F Barker, through whose courtesy this report is made

The *complaints* included dizzy spells for two years, usually associated with mild indigestion, a loss of 20 pounds in a year, and mild but increasing asthenia *Family history* unimportant *Past history* included an occasional sore throat and several attacks of chills and fever in childhood, no venereal disease, tonsillectomy five years ago following slight pain in a shoulder, good habits Twelve or thirteen years ago, during military drill in preparatory school, the patient was twitted on the large size of his upper abdomen Mild piles appeared once, and rarely, in late years, there had been a little bleeding from the gums Occasional mild indigestion with belching after meals

The *present illness* made itself felt about two years ago with a short attack of severe vertigo After eight months of freedom the attacks of vertigo became somewhat more frequent, though irregular in time One year ago the attacks became more intense and were sometimes followed by nausea and vomiting, about the same time there was a single episode of slight pain in

the other shoulder Recently, vertigo had occurred about once a month, usually when first going to bed, attacks were short, severe, and accompanied and relieved by copious vomiting, not of the projectile type, sometimes there was diplopia Of late there had been a growing lassitude, though intellectual interest in the daily work was undiminished

*Physical Examination*—Pyknic Dark complexion Skin of face, neck, and hands shows definite though not intense florid duskiness General hypotrichosis Conjunctivae clear Buccal and pharyngeal mucous membranes redder than normal Dulness at base of lungs posteriorly higher than usual, heart transverse, lungs and heart otherwise normal Pulse regular, 96 per minute Blood pressure 126/88 No peripheral sclerosis Upper part of abdomen a little prominent, area of stomach tympany a little increased, edge of spleen easily felt under left rib border, descending one fingerbreadth on inspiration, nontender, liver edge one to two fingerbreadths below costal margin, with a slight descent on inspiration, nontender Reflexes normal Rather marked venous engorgement in fundi

The *further diagnostic study* brought out the following points x-Rays revealed sound teeth, unusually high diaphragm, questionable defect in the prepyloric region of the lesser curvature Psychiatric examination (Dr L B Hohman) negative No disease in nose and throat (Dr E N Broyles) The ophthalmologist (Dr A L MacLean) reported slight conjunctival injection, chronic follicular conjunctivitis, and engorged retinal veins, slight muscular imbalance at one of three examinations *Laboratory tests* Blood Wassermann negative Gastric analysis normal Urine showed a very faint trace of albumin, rare hyaline cast, a little urobilinogen but no urobilin Blood Red blood cells, 8 673 million, hemoglobin, 120 per cent, white blood cells, 17,100, differential count, polymorphonuclear neutrophils, 78 per cent, eosinophils, 1 6 per cent, basophils, 1 2 per cent, small mononuclears, 11 6 per cent, large mononuclears and transitionals, 7 6 per cent Estimates of volume and viscosity of the blood and of the proportion of red cells to plasma were not made

*Diagnosis*—Polycythemia rubra vera with enlargement of spleen and liver

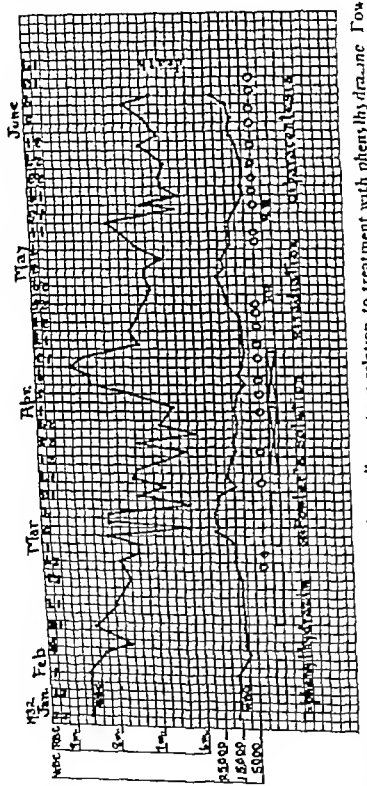


Fig 206—Erythremia Red and white cell counts in relation to treatment with phenylhydrazine Fowler's solution and radiation

*Later Course*—The accompanying chart (Fig 206) records the subsequent blood counts and the specific treatment

A total of 3 6 Gm of phenylhydrazine hydrochloride (0 1

Gm per day orally) was given between January 26th and March 14th, in courses of from ten to fifteen days' duration *February 6th* Considerable fresh blood reported passed per rectum, paresis of left arm and leg for only a minute or two, paresthesia front of both thighs ("as if sandpapered") and occasionally of left side of tongue *February 8th* Patient thinks ankles have been slightly swollen, no edema found, bled 400 cc from arm, with relief of neurological symptoms for nearly a week *February 15th* Two or three dizzy spells within a day or two, tonight the most severe vertigo yet *February 17th* Rather rapid enlargement of abdomen in past five days, fluctuation present, edema of ankles *February 23rd* Ascites somewhat increased, diuretin begun ($7\frac{1}{2}$ grains three times a day) with restriction of fluid intake (these measures seemed to have no effect) *February 26th* Ascites increasing, admitted to the Union Memorial Hospital for tapping

From this point on the patient remained in the hospital and his story is one of gradual decline An acute bronchitis developed on March 4th, the rise in the white cell count and fluctuation of the red cell count at this point are probably due to this infection and not to phenylhydrazine therapy, cough persisted for a week or two

On March 14th phenylhydrazine was discontinued because of therapeutic failure and of the persistence of marked ascites (necessitating frequent paracenteses, see chart) ascribed to a probable portal thrombosis On March 18th Fowler's solution was given in increasing doses, stabilized at 20 drops three times a day from April 6th to 12th The red count rose to its highest recorded point (8 8 millions) We expected a subsequent fall and reduced the daily amount of arsenic rapidly to zero, the fall occurred, but not to a satisfactory degree, and the condition of the patient remained the same

Since phenylhydrazine and arsenic had, we thought failed of sufficient effect, we turned to radiation On April 26th and 28th and on May 14th and 17th Dr Curtis F Burnam radiated the long bones (not the spleen), giving a total of 4000 r There was no reaction, either general or hematological The pa-

tient became slowly weaker, lapsed into coma, and died on June 17th

During his illness he was tapped twenty three times (between February 26th and June 14th) with a measured total drainage of 147 liters, much more ascitic fluid drained from the paracentesis wound between tappings—twice for as long as two weeks Collateral circulation was not evident Lemonade, rather strong vinegar and salty foods were craved by the patient, he enjoyed the old fashioned "switchel"—a hayfield drink of vinegar sugar, and water

On March 25th a sharp pain, with nausea and vomiting, necessitating relief by morphine, occurred in the lower midabdomen, no change in white count, pain disappeared after a few hours There was frequent complaint of bothersome "kinking" in the fingers The Chvostek and Trousseau signs remained negative

The liver edge retreated under the costal margin during the four months observation, it was never notably tender

*Autopsy* was permitted Positive findings included chronic passive congestion and multiple infarcts of the spleen, with chronic perisplenitis, thrombosis of the portal and hepatic vessels associated with hemorrhage, central necrosis, and early cirrhosis of the liver, mesenteric thrombosis with gangrenous changes in the ileum, marked dilatation of the diaphragmatic vessels and collateral circulation, hyperplastic bone marrow, markedly dilated stomach, with no sign of obstruction, terminal bronchopneumonia In addition—and totally unexpected—there was rheumatic endocarditis with small firm vegetations along the mitral valve (probably recent) with "relatively fresh" Aschoff bodies in heart and liver (Report from Union Memorial and Johns Hopkins Hospitals)

Discussion—In retrospect, this case affords ground for several bits of interesting speculation

*The relation of the rheumatic fever*, demonstrated first by the pathologist and not until then suspected, to the presenting disease is far from clear During the four months' period of observation the patient had had no pain nor any swelling of the

joints, there was no significant fever until the preagonal rise, and only once (January 27th) was even a suggestion of a systolic murmur heard Later, when Aschoff bodies had been demonstrated in the liver, one consultant suggested that rheumatic fever, through hepatic damage, had been at least the activating factor in the immediate picture To this view must be opposed the fact of the frequent occurrence in cases of polycythemia of precisely the complications found in this case (namely, portal thrombosis and cirrhosis of the liver) and the further fact that in thousands of recorded cases of acute rheumatic fever liver damage, portal thrombosis, and polycythemia have been absent It would seem justifiable to conclude that the rheumatic fever was fortuitous and merely added to the sum total of the patient's troubles, but it would be interesting to know why the clinical signs and symptoms of the rheumatic infection were so at variance with the pathologic findings

*The question of priority as between blood and liver changes* in polycythemia has been much debated, but no unanimity of opinion has emerged That liver changes are common has been proved by many autopsies, and Harrop[1] states that enlargement of the liver is recorded in at least one half of the clinical reports Brown and Giffin[2] found no relation between the size of the liver and the amount of blood in the body (although there did seem to be a definite relationship in the case of the spleen), and they feel that the hepatomegaly is not merely mechanical The nova that produces it may be extraneous to the liver, affecting the liver first and then, sequentially, the blood, or it may arise from the blood in the course of the unnatural hemolysis Levi[3] has well stated three views of the situation He quotes Hess and Saxl[4] as believing that there is a "loss of the hemoglobin-destroying function of the liver, by reason of alteration of the liver cells, with ensuing hyperglobulia" Turk[5] also held to a "primary disease of the liver and blood destruction by a toxin, with secondary overproduction of red blood cells in the marrow" Mosse,[6] on the other hand, felt that the polyglobulia was the primary factor and that the liver changes came about because of the plethora and the accompanying increased blood destruction

Others, remembering that circulatory disturbances of many kinds may give rise to a secondary polycythemia, believe that primary changes in the liver may induce thrombosis of the portal system and so cause a rise in the erythrocyte count More common, however, is the opinion that portal thrombosis is an expression of the heightened tendency of polycythemic blood to clot and is not necessarily a consequence of liver damage Chauffard and Troisier[7] report a case in which they believe cirrhosis was secondary to portal thrombosis

In the evaluation of these theories it must be kept in mind that there is perforce but little laboratory evidence to go on The onset of erythremia is insidious and the condition is usually well established before medical advice is sought Even then, as Christian[8] has pointed out, the patient's complaints are most often of difficulties referable to the nervous system, as in the present case We have no direct way of telling when changes in blood or liver set in, nor which antedated the other Observation, blood counts, and perhaps liver function tests for many years on a large series of persons would probably throw some light on the question, but these procedures are not usually practicable Accurate blood counts on successive classes of nurses and medical students might be of value eventually, if kept over a number of years, especially if those cases with high red cell counts were followed subsequently

On the whole it seems most reasonable to agree with Kratzeisen,[9] Harrop,[1] Hirshfeld,[10] Mosse,[6] Levi,[3] Gaisböck,[11] and others, that the blood changes are primary and that portal thrombosis and liver damage are secondary phenomena In the case here presented it must be acknowledged that there is slight and hearsay evidence of enlargement of the upper abdomen for at least twelve or thirteen years, and it is conceivable that this enlargement was due to hepatomegaly Even so, we cannot assume the priority of liver changes here, for we know nothing of the blood picture earlier than four months before death Our impression is that true polycythemia, possibly with mild hepatic changes, had existed for a number of years, and that the onset of portal thrombosis (possibly hastened by phenylhydrazine

therapy) was in some way responsible for the inception of more active changes in the liver, resulting in the necrosis and cirrhosis found at autopsy

A good deal has been written about *the effects, both good and bad of phenylhydrazine hydrochloride therapy* There is general agreement on the efficacy of the drug, in suitable dosage, in lowering the red cell count, the effect is ascribed to the actual hemolytic destruction of red cells, as determined clinically and biochemically (Altnow and Carey,[12] Huffman,[13] Giffin, Allen, and Barker[14]) On the whole, results with phenylhydrazine appear to have been better than with other forms of treatment (venesection, radiation, arsenicals, etc ) A number of cases are on record in which the red count has been brought to normal with this drug and kept there, by occasional courses of medication as necessary, for several years, with great resulting comfort to the patient Unfortunately, in the course of treatment, untoward developments have at times occurred in chronological if not in causal sequence

The commonest of these sequels is undoubtedly thrombosis, most often seen in the portal system, but occurring elsewhere as well It must be remembered, on the one hand, that thrombosis is common in untreated polycythemia, and, on the other, that phenylhydrazine has been given over long periods without the appearance of thrombosis One cannot prove that thrombosis following phenylhydrazine is caused by the drug, yet, almost without exception, investigators have emphasized their belief in an increased tendency to thrombosis after administration of phenylhydrazine (Allen,[15] Horton[16]) and warn against its use when any evidence of thrombosis is already present and in older persons or those with arteriosclerosis We find ourselves then in a dilemma, for in the very treatment of erythremia which promises most in the way of comfortable control of the disease lurks the threat of the thrombus

Again, with regard to *the possible toxic effects of phenylhydrazine on the liver*, there is, at present, but little conclusive evidence Giffin, Allen, and Barker[14] in their experiments on normal dogs found that huge doses caused but little hepatic or renal damage,

even lethal doses produced only some atrophy of the hepatic cells, especially round the central veins and the portal spaces Huffman[13] could demonstrate no serious renal or hepatic injury It has been remarked, however that the normal liver of the dog may differ considerably from that in a human case of polycythemia, and Levi[2] sums the matter up well when he concludes that destruction of blood somehow damages the liver and that repeated courses of phenylhydrazine may therefore give rise to cirrhosis

In the case here discussed, the liver was slightly enlarged before the exhibition of phenylhydrazine, but there was no sign of jaundice nor of portal obstruction Icterus, in fact never appeared, but evidence of portal thrombosis did appear after only 1 8 Gm of phenylhydrazine hydrochloride had been given (over a period of eighteen days) This is a small amount Moreover, it had produced, at that time, no leukocytosis no marked fall in the red cell count, no appearance of normoblasts or myelocytes in the circulating blood, and no icterus, it does not seem, therefore, that the patient had any undue sensitivity to the drug The total dose of 3 6 Gm in a period of forty-eight days seems also too small to cause liver damage It may be that phenylhydrazine was responsible for the development of the portal thrombosis and the hepatic necrosis and cirrhosis, but it may equally well be that the exhibition of the drug merely coincided with changes that would have appeared in any case. The subsequent apparent inefficacy of arsenic and radiation, given, it seemed to us in adequate dosage, perhaps indicates that the disease was unusually resistant to any form of therapy, on the other hand, it might have been possible to secure definite improvement with phenylhydrazine if thrombosis had not supervened The situation emphasizes the imperative need of close individual study of every separate case with individualization of the treatment—but of what disease is not this true?

In closing, two or three additional points of especial clinical interest may be mentioned When the red cell count was highest (8 8 millions) and only then, the patient complained of severe burning of the eyeballs The conjunctivae were slightly injected

but there was no sign of inflammation I find this symptom spoken of by only one writer (Leopold[17]) and believe that it should receive more attention It may possibly be due to the engorgement of the fundal veins

In spite of the twenty-three paracenteses made at very frequent intervals (Drs Gibson and Grimes), autopsy revealed only one small omental adhesion to the abdominal wall—added evidence, if any be needed, that tapping done carefully and gently may be repeated many times without serious local disturbance The patient always felt better when, after a tapping, the fluid was allowed to accumulate again, continued drainage from the paracentesis wound always resulted in a feeling of weakness Frequently, also, the patient craved acid, sour, and salty foods and drinks

Summary —A case, believed to be erythremia (polycythemia rubra vera), is presented in which portal thrombosis with ascites appeared soon after the beginning of therapy with phenylhydrazine Arsenic and radiation seemed to have but little effect upon the erythrocyte count Gradual decline Death in coma Autopsy report with discovery of previously unsuspected rheumatic endocarditis in addition to the usual findings in erythremia

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See also monographs by F Parkes-Weber (Hoeber, 1922) and Gaisböck (1922) and the article by Fitz in Oxford Medicine vol 2 part 2 p 763

## CLINIC OF DR HARVEY G BECK

MERCY HOSPITAL

### A CASE OF STATUS THYMICOLYMPHATICUS WITH ORTHOSTATIC ALBUMINURIA

A boy of fifteen in whom renal disease was suspected but later proved to be a case of orthostatic albuminuria associated with a constitutional abnormality of the thymicolymphatic type

Today I have the opportunity of presenting an interesting case of functional albuminuria occurring in a neuropathic individual with a constitutional anomaly The patient is a school boy fifteen years old He was admitted to the Mercy Hospital ten days ago complaining of breathlessness on exertion dizziness, and "tired feeling" He weighed 7½ pounds at birth For the first five months he was breast fed, after that he was fed on cow's milk and fruit juices His first teeth erupted at four months and he began to walk and talk before he was a year old At the end of his first year he was desperately ill for three weeks with cholera infantum During the following summer he was weak, emaciated, and unable to walk The mother states that he remained weak lifeless, and dull until he entered school at the age of six He got along fairly well in school the first year As a result of enlarged tonsils and adenoids he was a mouth breather and suffered from frequent attacks of sore throat Upon the advice of the school physician he entered Maryland General Hospital where the tonsils and adenoids were removed He did not react well from the ether anesthesia and the operation From noon (time of the operation) until 7 A M the next day, he remained unconscious except for a few minutes at 7 P M when he aroused sufficiently to cough several times He was confined to the hospital five days For

the next two years he was treated in the dispensary clinic for some condition of the heart During this period, attendance at school, participation in games, or any sort of physical exercise was prohibited, and up to the present time, he has not indulged in play on account of breathlessness on exertion

Eight months after the operation he began to suffer with attacks of dizziness In several he lost consciousness, which lasted from fifteen to twenty minutes At first they occurred daily, then averaged two or three a week Later he was free from attacks for intervals of three or four months The last one occurred three years ago The attacks were precipitated by overexertion, excitement, or sudden emotions, especially fear He recounts one attack which occurred while walking on a log across a stream, another (which lasted four hours) when he had a tussle with a boy, again others while riding in street cars The seizures were ushered in by pallor of the face, a sense of giddiness and uneasiness in the epigastrium During the attacks the mother noticed that the lips turned blue and became swollen, the extremities became cold and bathed in perspiration, and he appeared to struggle for his breath The respiratory effort was so pronounced that the whole bed would shake They were not accompanied by any convulsive movements, biting of tongue or incontinence of urine Vomiting occurred occasionally after the attacks, cyanosis and swelling of the lips was common On careful inquiry it was ascertained that he was a neurotic individual He has always been fretful, irritable, and emotional, and easily driven to tears He worried over inconsequentals and became introspective The latter was, no doubt, due to the fact that his attention had been directed persistently to his heart during the two years he was treated at the dispensary As a result, he became heart conscious Frequently he would place his hand over the precordia in order to feel the pulsation He also developed the habit of biting his nails Certain fears developed, particularly the fear of heart disease In fact, this fear amounted to an obsession so that he was unable to concentrate on his studies in school with the result that he had to repeat his second and fourth grades and failed in his seventh grade As

he had been cautioned against overexercise on account of his heart he lost all interest in play and outdoor sports This lack of diversion and exercise contributed further to his neurosis He always feels tired and lacks endurance and initiative

Sexually he appears immature There has been no awakening of the normal impulses for his age At the age of eight he began smoking cigarettes A year later he discontinued until two years ago when he resumed the habit Since then he has smoked on an average four cigarettes a day

The family history is unimportant

He has a splendid appetite good digestion, and spontaneous bowel movement daily

His chief cardiorespiratory symptoms are breathlessness and palpitation on physical exertion, and a nonproductive cough of six months' duration

Although albumin was found in the urine some months ago, for which he was referred to the hospital, he has had no genito urinary symptoms suggesting nephritis such as pollakiuria, nocturia oliguria, or dysuria

**Physical Examination**—The patient is imperfectly developed He is normal in weight and in stature, and skeletally appears pretty well proportioned However, he has a low, receding forehead and the anteroposterior diameter of the skull is increased The angles of the scapulae stand out prominently and there is a well-developed lumbar lordosis with marked flexibility of the spine and hyperextensibility of the joints of the extremities The skin is soft in texture and the hands and feet are bathed in cold perspiration. He has a good growth of hair on the scalp, normal eyebrows and long eyelashes, but there is no suggestion of any hair on the face Axillary and pubic hairs are abundant, the latter show a feminine distribution with an upper horizontal border The genitals are underdeveloped but the breasts are prominent Other developmental defects are abnormally small ears, narrow, high arch palate, large upper central incisors and separation of the recti muscles Among the most outstanding features are a group of vasomotor phenomena These include morbid flushing of face and neck, dermatographism, cold clammy

hands, deep, purple congestion of hands and turgescence of veins while standing with the arms lowered along the side of the body and pallor and collapse of the veins with the arms raised above the head

Aside from the excessive growth of lymphoid tissue in his early life—hypertrophied tonsils and adenoids (which were removed by operation), he still manifests evidence of general lymphatic hyperplasia in the nature of enlarged lymph glands in the cervical, axillary, inguinal, and femoral areas The thyroid is not palpable The heart and lungs appear normal The abdomen presents an enteroptotic habitus with rectus diastase and an atonic and ptosed stomach which exhibits a splashing sound on percussion four hours after a meal and extends two fingerbreadths below the umbilicus The spleen and kidneys are not palpable and the liver is not enlarged Reflexes are normal

Roentgenograms of both hands show delayed epiphyseal union in all of the phalangeal and metacarpal bones These should normally be closed before the end of the fifteenth year A film taken of the chest did not show any abnormal shadows

**Laboratory Studies** — *Urine* —On the day of admission the urine contained albumin (1 plus) and an occasional granular cast Subsequent specimens collected while the patient was resting in bed were all negative for albumin, although some of them contained occasional granular casts No other abnormalities were found in a series of nineteen examinations No casts were found in the later specimens The specific gravity ranged from 1 010 to 1 022 In the kidney concentration test it rose to 1 031 and in the dilution test it dropped to 1 006 Because of the postural influence on venous congestion, the result of an unstable vasomotor nervous system, the following studies were undertaken to determine the postural influence on albuminuria

First specimen 12 to 1 P M , recumbent posture after dinner (−)

Second specimen 1 to 2 P M , sitting posture (+ −)

Third specimen 2 to 3 P M standing posture (++++)

Fourth specimen 3 to 4 30 P M , recumbent posture (+)
Fifth specimen 6 to 7 P M recumbent posture (−)

Note The 1 plus albumin in fourth specimen probably represents the residual albumin from the kidneys after the third specimen was voided

In the intravenous sulphophenolphthalein test 60 per cent of the dye appeared in the urine at the end of the first hour and 68 per cent at the end of the second hour

*Blood Chemistry* —Blood sugar, 129 mg per 100 cc of blood, urea 32 mg per 100 cc of blood, urea nitrogen, 15 mg per 100 cc of blood, chlorides 280 mg per 100 cc of blood, sodium chloride 462 mg per 100 cc of blood, cholesterol, 140 mg per 100 cc of blood

Total plasma proteins, 7 5 Gm per 100 cc plasma, fibrinogen, 0 4 Gm per 100 cc plasma, albumin, 4 6 Gm per 100 cc plasma, globulin, 2 5 Gm per 100 cc. plasma

*Albumin-globulin* ratio, 1 85

*Blood Wassermann* negative

*Blood Count* —Hemoglobin, 90 per cent, erythrocytes, 4 800 000, leukocytes, 8350, polymorphonuclears, 73, small lymphocytes, 15, eosinophils 6, basophils, 1, large mononuclears, 4, transitionals 1

*Stool* —Negative

*Basal Metabolic Rate* —Minus 22 per cent

From the laboratory studies it will be observed that special attention was directed to an investigation of the kidneys in the hope of establishing some organic lesion characteristic of nephritis to account for his albuminuria However, none of the tests were indicative of nephritis The urine besides containing considerable albumin occasionally contained a few granular casts Occasionally the latter appear in functional albuminuria No other abnormalities were found

The sulphophenolphthalein test was normal but there was a slight delay of excretion in the water dilution test and a variation of 6 degrees in the specific gravity in the concentration test Churchman reported a case of status thymicolymphaticus in which the Volhard water test showed delayed excretion with a

normal range of concentration The blood chemistry which included quantitative determination of urea, urea nitrogen, sodium chloride, and cholesterol were all within normal physiologic limits Blood sugar was somewhat above the average normal

The plasma proteins were also normal in amount and the albumin-globulin ratio was normal

The blood count showed no evidence of anemia and the differential count was normal except for a slight increase of eosinophils

It is clearly evident from these laboratory findings that if there are any structural changes in the kidneys they are not sufficient in the absence of any material impairment of renal function to account for the rather unusual and prolonged train of symptoms from which the patient complains The disease is, therefore, not strictly a nephropathy and the albuminuria must be of a functional nature There are many forms of functional albuminuria but, inasmuch as the vasomotor manifestations are the most outspoken symptoms and as vasomotor phenomena are constantly present in so-called "orthostatic albuminuria," it was decided to note the postural effect on blood pressure as well as on albuminuria

Many years ago I made a series of observations on the postural influence of blood pressure in patients suffering with vasomotor disturbances, including cases of orthostatic albuminuria with the aim of determining the degree of variation from normal as expressed in units of millimeters of mercury The results showed that the pressure was invariably higher in the recumbent posture than in the upright, and with the patient sitting erect, there was a marked variation of pressure when the arm was elevated as high as possible without exerting tension on the large vessels, and when it was in a dependent position along the side of the body The difference usually amounted to 30 or 35 mm of systolic pressure and, in one instance, as much as 50 mm , whereas in normal healthy individuals it rarely exceeded 20 mm

In this patient the systolic pressure taken with the arm in the usual position was 8 mm higher in the horizontal posture

than in the sitting posture In the latter it was 42 mm lower with the arm elevated than with the arm hanging down

The blood pressure reading with the arm raised was systolic 86 and diastolic 56, and with the arm dependent systolic 128 and diastolic 90 This variation denotes a marked degree of instability of the vasomotor nervous system which accounts for such symptoms as dizziness, vertigo, breathlessness, palpitation, sweating, acrocyanosis lividity alternating with pallor and turgescence of veins, and it may also account in some way for his syncopal attacks, cardiac neurosis, and postural albuminuria Since vasomotor instability, like albuminuria, is only a symptom and not a clinical entity, further searches were instituted which involved studies of the individual as a whole These necessitated an investigation of the heredity, environment, constitution, and personality No factors contributing to his symptomatology can be ascribed to either heredity or environment His antecedents do not give a history or show any evidence of any constitutional anomalies or hereditary diseases and there is nothing in his habits or environment which could be responsible for his symptoms As to his constitution and personality, there is positive proof of some deviation from the normal. He presents a fairly definite clinical picture of a lymphatic diathesis or what is now known as status thymicolymphaticus This type of constitution is characterized by many of the signs and symptoms which he presents, namely, faulty osseous development with delayed epiphyseal closures, late puberty, hypogenitalism, feminine features with heterosexual distribution of pubic hair, absence of hair on the face, well-developed breasts, narrow highly arched palate, large upper central incisors, enteroptotic habitus, lumbar lordosis, hyperextensile joints, lymphatic hyperplasia and other developmental defects The blood usually shows some lymphocytosis and a mild degree of eosinophils, and albuminuria of the orthostatic variety frequently coexists Upon this constitutional basis the subjective symptoms from which this patient complains developed These comprise practically the entire category which characterize this biological type of individual It is

reasonable to assume that the profound shock sustained from a simple operation, the vertiginous and syncopal attacks from which he subsequently suffered, the flushing, sweats, cyanosis, pallor and breathlessness after exercise or exertion, the fatigability, cardiac neurosis, and lack of emotional inhibition are all manifestations which can be attributed primarily to disturbances of the function of the thymus gland The attacks accompanied by respiratory distress and signs of suffocation (such as lividity or cyanosis) were particularly suggestive of thymic stridor although they usually appear at an earlier age

The reason why this case was not recognized earlier as one of status thymicolymphaticus is due to the fact that it is difficult to do so before the age of puberty The features are more distinct in adults after the appearance of the secondary sex characters The only evidence lacking to make the clinical picture complete is the absence of cardiac and aortic hypoplasia and roentgenographic evidence, of an enlarged thymus However, a committee appointed to investigate the nature of status thymolymphaticus reported that it has been pretty well established that the size of the thymus has not much to do with sudden death as was formerly supposed and that a large thymus alone does not indicate status thymicolymphaticus According to Falta, the heart may be hypertrophied During acute attacks it is usually dilated Clinically an enlarged thymus is not often recognized and roentgen rays do not always show the abnormal size of the gland The present trend is to ascribe the symptoms to some hormone as yet undetermined In all of these cases there may develop a compensatory disturbance in the thyroid, pituitary, and adrenal glands as Timme has pointed out This fact doubtless explains the low basal metabolic rate of minus 22 per cent However, his mental alertness and general symptoms do not suggest such a low rate Engelbach observed that disturbance of the function of the thyroid gland in these individuals tends to hypothyroidism before puberty and to hyperthyroidism in the adult

The hypogenitalism with retarded and lessened sexual instinct and heterosexual tendency results from a secondary

hypopituitarism with deficiency of the sex stimulating hormone Likewise his abnormal emotional reactions, his sensitive, unstable vasomotor mechanism (as indicated by flushes, sweats, and fluctuating blood pressure) and his feeling of exhaustion are probably secondary to suprarenal insufficiency As previously mentioned, functional albuminuria of the postural variety is frequently a symptom of this complicated clinical picture A strikingly similar case of a girl sixteen years of age is at present under my care She exhibits the same developmental defects, based on endocrine disturbance of the thymus, pituitary, and adrenal glands, with delayed puberty, childish mannerisms, and retarded mental development She also has outspoken vasomotor disturbances, marked lumbar lordosis and orthostatic albuminuria

Numerous causes have been ascribed to orthostatic albuminuria Many authorities attribute it to a mechanical interference of the circulation in the kidneys as a result of pressure from lumbar lordosis which is frequently present, others, to torsion of the renal vessels occurring in movable prolapsed kidneys or abnormally small renal vessels due to vascular hypoplasia such as occurs in the heart and aorta Again others consider it as one of the many manifestations of a vasomotor neurosis Inasmuch as all of the factors enumerated are concerned in the production of the clinical picture of status thymicolymphaticus there has developed among the leading clinicians a group who adhere to the view that orthostatic albuminuria is a manifestation of a faulty or abnormally developed constitution

Individuals suffering from this disease always show lack of emotional inhibition Strong emotions are capable of producing albuminuria This has been demonstrated experimentally by subjecting cats to severe fright and pain which causes albumin to appear in the urine Wallis observed among English school boys that those who fainted in chapel were more likely to have albuminuria It would have been interesting if an examination for albumin could have been made in our patient after one of his emotional episodes

Orthostatic albuminuria has also been looked upon as a sequel to acute nephritis, especially following scarlet fever Postural

changes in pulse pressure, increased permeability of the renal vessels and changes in the composition of the blood due to disturbed calcium metabolism have been mentioned as possible etiologic factors

There is an unquestionable predisposition in the particular type of individuals to which this patient belongs The albuminuria usually occurs during the period of most rapid growth and subsides spontaneously in early adolescence

**Comment**—The patient presented did not reveal any definite clinical or laboratory evidence of true nephritis as exhaustive as these studies have been made It was not until a careful investigation was made into the background for hidden, underlying factors relating to his constitutional pattern and personality that sufficient facts were revealed upon which a diagnosis could be established Aside from the clinical interest this case possesses, it serves to emphasize the importance of studying the fundamental biological factors—heredity, environment, constitution and personality, in their relation to health and disease in every individual suffering from a chronic malady

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